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SEPTEMBER, 1929

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American Journal of Diseases of Children

VOLUME 38 SEPTEMBER, 1929 NUMBER 3

EPILEPSY IN CHILDREN

THE RELATIONSHIP OF WATER BALANCE TO THE OCCURRENCE OF SEIZURES *

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ROCHESTER, N. Y.

The fact that seizures can usually be prevented in epileptic children by fasting [1] or by diets relatively low in carbohydrate and high in fat [2] has interested us during the past three years, largely as a starting point for a study of the etiology of this disorder. We have investigated various phases of the problem with the assumption that any knowledge of the physiologic alterations produced by favorable therapeutic regimens might lead to a better understanding of the basic disturbance present, just as information regarding the effects of the seizure itself might give a clue to its mechanism. The present report is concerned with changes in the water balance of the body, a phase of the subject which is intimately related to other angles covered in previous communications from this clinic.

The possible importance of this aspect of the problem was first suggested to us by the fact that the major portion of the decrease in body weight during periods of fasting is due to loss of water. This has been

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* From the Department of Pediatrics, the University of Rochester and the Pediatric Service of the Strong Memorial Hospital.

* Presented in Abstract at the Annual Meeting of the Eastern Pediatric Research Society at Boston, March 23, 1929.

* Read before the American Pediatric Society, St. Louis, May 22, 1929.

* This study was aided by grants from the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation and by an anonymous donor.

1. Guelpa, G., and Marie, A.: La lutte contre l'épilepsie par la désintoxication et par la rééducation alimentaire, Bull. gén. de thérap. **160**:616, 1910. Geyelin, H. B.: Fasting as a Method for Treating Epilepsy, M. Rec. **99**:1037, 1921. Conklin, H. W.: The Cause and Treatment of Epilepsy, J. Am. Osteopath A. **22**:11, 1922.

2. Wilder, R. M.: The Effects of Ketonuria on the Course of Epilepsy, Mayo Clinic Bull. **2**: 307, 1921. Peterman, M. G.: Ketogenic Diet in the Treatment of Epilepsy, Am. J. Dis. Child. **28**:28 (July) 1924. Talbot, F. G.; Metcalf, K., and Moriarty, M.: The Ketogenic Diet in Treatment of Idiopathic Epilepsy, abstr., Am. J. Dis. Child. **32**:316 (Aug.) 1926. McQuarrie, Irvine; and Keith, H. M.: Relationship of Variations in the Degree of Ketonuria to Occurrence of Convulsions in Epileptic Children on Ketogenic Diets, Am. J. Dis. Child. **34**:1013 (Dec.) 1927. Helmholz, Henry F.: The Treatment of Epilepsy in Childhood, J. A. M. A. **88**:2027 (June 25) 1927.

observed by a number of investigators, but it was shown most strikingly by Gamble, Ross and Tisdall [3] in their intensive study of the metabolism of fixed base during fasting. That diets extremely low in carbohydrate and relatively high in fat have a similar dehydrating effect was first shown by Stark [4] in 1769. Other workers [5] have amply confirmed this observation. An additional fact which suggested the desirability of investigating the possible relationship of a disturbance in water balance in epilepsy is that mild polyuria usually follows the seizure. This was demonstrated by Gamble and Hamilton [6] in a careful study on one patient who had seizures in series at weekly intervals. Patients or their parents not infrequently volunteer history confirmatory of this observation. The usual explanation of the phenomenon is that extra water is excreted incidental to the removal by the kidneys of catabolites formed during the seizure.

The foregoing considerations, together with the hope of adding the acidosis-producing effect of dehydration to our therapeutic regimen, led us early to advise a moderate limitation of the fluid intake in occasional patients who responded unsatisfactorily to the ketogenic dietary alone. One of these patients followed in the outpatient department during the early months of 1928 improved so strikingly when placed on a restricted water intake in addition to the ketogenic diet, that other patients with more severe cases were soon treated in a similar manner with satisfactory results. A few attempts at controlling seizures of patients on ordinary high carbohydrate diets by restriction of fluids alone were much less successful, but this result was probably due to the fact that the degree of restriction was not sufficiently great and the periods of trial were too short.

The present orientation study was undertaken to determine, if possible, the true relationship of water balance to the occurrence of seizures with the hope of shedding some light on the underlying factors involved in the disease itself.

PLAN OF STUDY

The simple method followed was that of observing frequency and severity of convulsions and the occurrence of other symptoms in epileptic children when they were placed on different levels of water intake. In

3. Gamble, J. G.; Ross, G. S., and Tisdall, F. F.: The Metabolism of Fixed Base During Fasting, J. Biol. Chem. **57**: 633, 1923.

4. Stark, W., in Lusk, G.: The Science of Nutrition, ed. 4, Philadelphia, W. B. Saunders & Company, 1928.

5. Bischoff, T. L. W., and Voit, C.: Die Gesetze der Ernährung des Fleischfressers, Leipzig and Heidelberg, 1860, pp. 211 and 214. Benedict, F. G., and Milner, R. D.: Bull. 175, U. S. Dept. Agric., Office of Experiment Stations, 1907, p. 224.

6. Gamble, J. L., and Hamilton, B.: The Acid-Base Composition of Urine from an Epileptic Child, Bull. Johns Hopkins Hosp. **61**: 389, 1927.

order that results from the relatively short periods of observation might be of significance, only subjects suffering from unusually severe, so-called idiopathic epilepsy were selected for the investigation. The special experiments were carried out with the full cooperation of the patients and their parents. The output of water was determined by accurate measurement of the urine collected at frequent intervals and by changes in body weight. The intake was calculated to be that contained in the diet, as estimated from standard food tables, plus the amounts allowed as drinking water. The water of metabolism of the food has not been considered in this first study because it was felt that the general method employed was not sufficiently accurate to require this refinement. In order that the specific effects of the diet used might introduce the minimum degree of error, the total number of calories allowed was that calculated to be required for maintenance of body weight under ordinary conditions with proper quantities of protein, fat and carbohydrate to insure nitrogen balance and a mixture of ketogenic and ketolytic constituents in most instances at or near the borderline of ketosis. As a check on the variations in concentration of the urine, the range of the specific gravity was determined. Rectal temperature was measured regularly in all cases throughout the period of study. The effects of antidiuresis as produced by solution of pituitary or by the administration of solution of the antidiuretic hormone of the hypophysis (betahypophamine) have been determined a number of times, both with the intake of water restricted and with it increased. Lastly, the effectiveness of the natural diuretic, urea, as an agent for removal of excess water under these conditions has been tested. With occasional exceptions, the patients have been kept in bed throughout the periods of study. No sedative drugs were given with the regimens used.

RESULTS OF EXPERIMENTS

For the sake of brevity and clearness, the results obtained are presented in graphic form on the following charts.

Experiment 1.—The data described in chart 1 suggest the following tendencies: (1) for the epileptic subject to retain body water to an abnormal degree during the active phase of the disease; (2) for seizures to follow the accumulation of water beyond a certain point; (3) for disappearance of seizures following the removal of extra water by rigid restriction of fluid and (4) for hyperthermia to occur from excessive restriction of water.

W. P., a boy, aged 6, was referred to the hospital as an emergency case, because he had been having from ten to thirty convulsions daily for a period of nearly two weeks in spite of fairly vigorous antiepileptic medication. Fluids had been forced during portions of this period. Petit mal seizures had been observed for the first time nine months previously and typical epileptic convulsions about seven months

before admission. These had been kept fairly well under control, however, by the use of moderate-sized doses of phenobarbital up to the time of the present outburst. In all other respects the patient was apparently entirely normal, both physically and mentally.

For the first few days after admission to the hospital the ordinary forms of sedative medication (magnesium sulphate intramuscularly, phenobarbital by mouth) tended to lessen the frequency and severity of the convulsions, but they still occurred in considerable numbers and his mental state was one of mild confusion or delirium throughout most of the intervals. During this period fluids were forced parenterally by the physician in charge, due to a slight elevation of temperature. Because the results of these procedures were unsatisfactory, all medication was discontinued and nothing whatsoever was given but 30 Gm. of 18 per cent cream by mouth every four hours night and day for three days. Data for the first day of this regimen

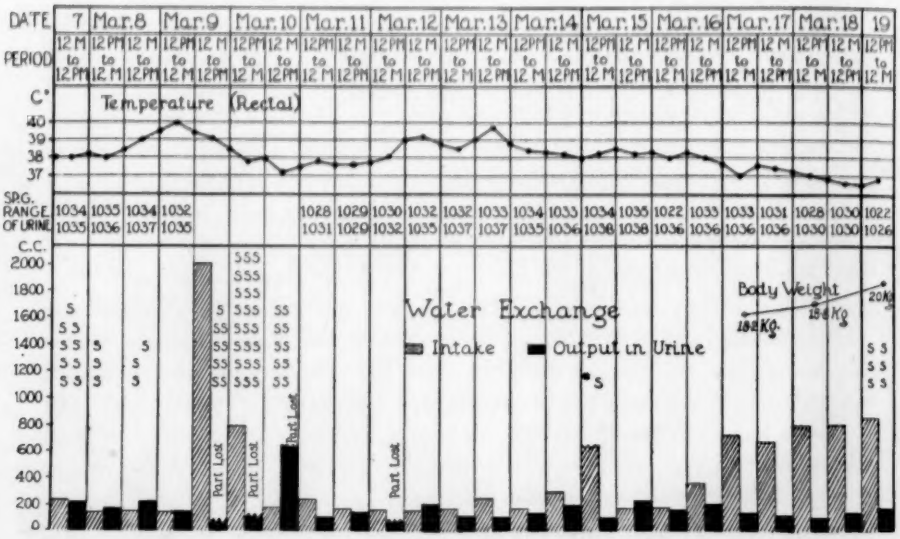

Chart 1.—Effects of different levels of water intake on the occurrence of seizures (*S*) and on changes in body temperature and body weight in W. P., a boy, aged 6 years. A borderline, nonketogenic diet was employed up to the nineteenth twelve hour period; a mildly ketogenic diet thereafter. The asterisk indicates when a large soap suds enema was given.

are not recorded on the chart. Those that follow, however, show an apparent tendency toward diminution in the frequency of seizures. None occurred during the last twelve hour period. Following this extreme restriction of water intake, however, the body temperature gradually rose to 40 C. and the mildly delerious state continued. Because of uncertainty as to the real origin and significance of the fever, it was thought advisable to force fluids according to the usual routine in other febrile conditions. The administration of 2,000 cc. of water during the next twelve hour period and 800 cc. during the first part of the second was followed by forty-three convulsions within a space of twenty-six hours. Rigid restriction of fluid intake, which was ordered after the seizures had begun to occur with great frequency, was followed within less than twelve hours by cessation of seizures. The

patient then remained entirely free from attacks for eight days except for one mild convulsion in the early morning of the fifth day. This occurred a number of hours following a large soap-suds enema, a large part of which the special nurse reported to have been retained.

Because of the recurrence of mild elevations in body temperature and because of the discomfort which accompanied the extremely low intake of fluid during the second period of dehydration, the attempt was made to determine the optimum allowance of water in preparation for the patient's discharge from the hospital. The volume being given was, therefore, first doubled and then quadrupled. At the same time the diet, while remaining isocaloric, was made mildly ketogenic (protein, 30 Gm.; carbohydrate, 20 Gm.; fat, 100 Gm.), whereas it had previously been nonketogenic. In spite of this moderate increase in the allowance of water and the change in diet, the volume of urine remained low and its specific gravity high.

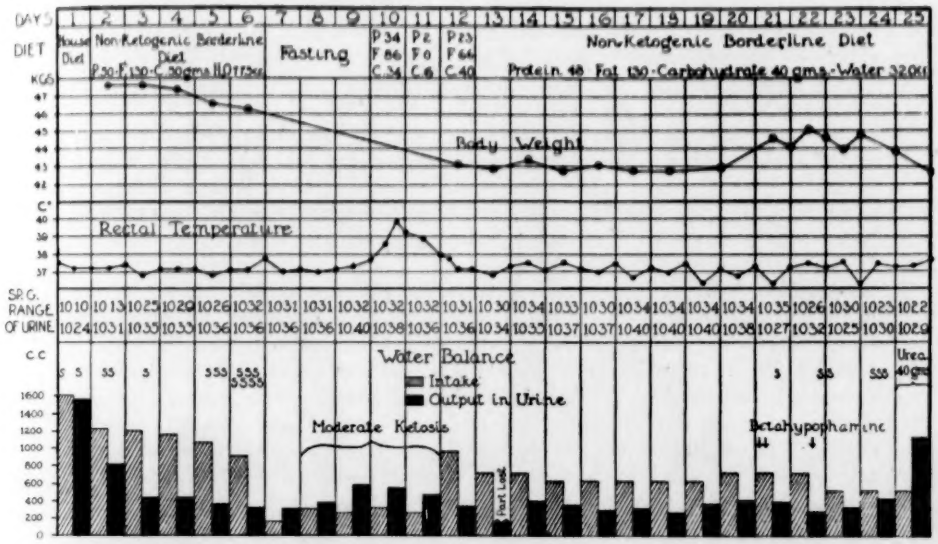

Chart 2.—Effects of various methods of dehydrating the body (restriction of water, fasting and urea diuresis) on the occurrence of seizures (*S*); effect of the antidiuretic substance of the posterior lobe of the hypophysis during the period when water was restricted in M. P., a girl, aged 14 years.

A gain in body weight from 18.2 to 20 Kg. within the same period indicated that nearly half of the water given had been retained. On the fourth day, six convulsions occurred within twelve hours. Restriction of water was again followed by cessation of seizures. A level of water intake between the two extremes tried was later found to satisfy the patient's physiologic requirements to all appearances and at the same time to prevent seizures entirely, even when the diet was of the nonketogenic borderline type with an energy value sufficient to permit normal growth and development.

Experiment 2.—The observations recorded on chart 2 show six points of special interest. 1. Unless the restriction of water is extremely stringent, initial control of seizures by this method alone in

a severe case may require an extended period, apparently because of a strong tendency for retention. 2. A regimen of fasting plus rigid restriction of water intake is extremely effective in causing a negative water balance and cessation of seizures. 3. This procedure results in hyperthermia and a rapid loss of weight, which might be harmful, if prolonged far beyond the period necessary for ridding the body of excess water and causing a cessation of seizures. 4. On an entirely adequate borderline nonketogenic diet, water balance can be established at a level which will prevent seizures and at the same time be compatible with comfort and normal physiologic activity. 5. Even in this state of relatively low water intake, body weight is increased and seizures are made to recur following the administration of the antidiuretic hormone, beta-hypophamine. 6. Such retained water is efficiently removed by large doses of concentrated urea solution, a procedure which is likely to be followed by cessation of seizures.

An Italian girl, M. P., aged 14, on whom we have made many different experimental studies during the past three years, was used for this series of observations. Under ordinary home conditions of diet and allowance of water, without large doses of phenobarbital, she was known to have from one to eighteen convulsions daily. These were often extremely severe and averaged from two to five a day. She was in this state when readmitted for the present study. The chart shows that she was entirely free from seizures so long as she was kept on the regimen of low water exchange alone. One of the striking features observed but not represented on the chart was the variation in emotional and mental reactions at different periods. When allowed to have convulsions, she was always dull, stubborn and exceedingly hateful, whereas during intervals of freedom from seizures she was cheerful, alert and cooperative. The one exception to the latter statement occurred during the two days of hyperthermia following the fast, when she was uncooperative and refused the major portion of her food. Except for the short period of ketonuria occurring with the fast, the urine remained negative to the qualitative ferric chloride test throughout the entire time.

Experiment 3.—Chart 3 shows the favorable effect of the restriction of water and also the tendency for seizures to occur in the presence of a positive water balance in the body.

E. M., an obese girl, aged 10, had suffered from epilepsy of increasing severity for about three years. Although she was the most mildly epileptic patient of the present series, she was having an average of at least one mild convulsive seizure daily at the time of admission, even when taking small doses of phenobarbital. She was immediately placed on a nonketogenic maintenance diet, which, however, kept her near the borderline of ketosis (protein, 50 Gm.; carbohydrate, 50 Gm.; fat, 130 Gm.). Some acute diuretic experiments were carried out during the first three days, after which she was placed on a regimen of restriction of water for one week. Water alone was then given in excessive amounts for two days, after which it was given in conjunction with a solution of pituitary (from 0.4 to 1 cc. every four hours). Following this experiment, a level of water balance was established which satisfied the patient's requirements and successfully prevented her seizures so long as she remained faithful to the regimen.

The striking feature is that seizures tended to recur when the ingestion of large amounts of water was not followed by loss of similar amounts. During the eleventh and twelfth days the excess of water taken was apparently excreted almost quantitatively, as may be judged from the weight remaining stationary, and no seizures occurred. Incidentally, this part of the experiment indicates that a strong tendency to retain extra water is not necessarily present at all times During the following two and a half days, however, when the same rate of water ingestion was continued along with periodic injections of solution of pituitary, water was retained as indicated by a substantial gain in body weight, and a status of seizures followed. She had never before this time had such severe seizures and had never been in status epilepticus. The convulsions were checked at the end of fifty minutes by the administration of chloroform, after which the water intake was again rigidly restricted. The markedly concentrated urine of the dehydration periods occasionally showed a faintly positive reaction to the ferric chloride test for aceto-acetic acid

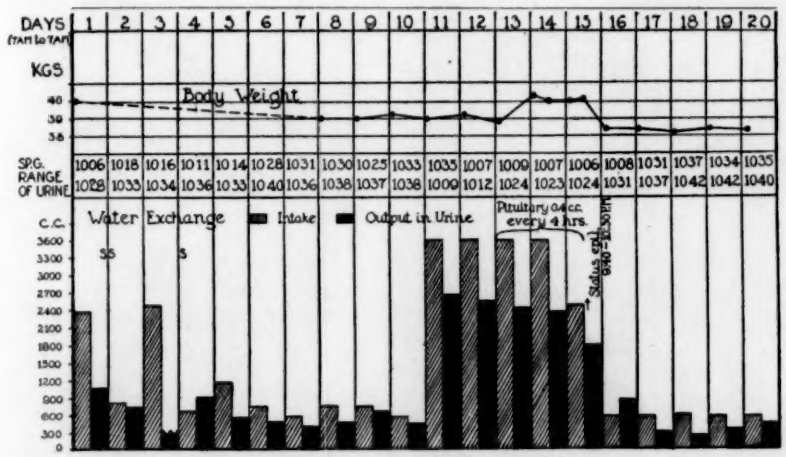

Chart 3.—Relationship of seizures (*S*) to the variations on the water exchange produced by restriction of water and forcing of water; also effect of solution of pituitary in connection with the forcing of water in E. M., a girl, aged 10 years. A borderline, nonketogenic diet containing 50 Gm. each of protein and carbohydrate and 130 Gm. of fat was employed. Status epilepticus was controlled by use of chloroform after fifty minutes.

in the specimens collected during the late afternoon, but quantitative estimation of the twenty-four hour excretion of total acetone bodies showed no definite increase over normal values.

The results of a closer analysis of the data obtained immediately before and after, as well as during, the time of this acute experiment, involving the simultaneous forcing of fluids and administration of solution of pituitary, are recorded on chart 4. The arrangement of the data in three-hour periods brings out the probable relationships more distinctly. It is seen that the antidiuretic effect of the pituitary was most marked during the three-hour period preceding the occurrence of

convulsions and that the status of seizures was followed by a comparatively large negative water balance and loss of weight during the four succeeding periods.

Experiment 4.—Chart 5 shows the relationship of different levels of water intake and output to the occurrence of convulsions when different diets were given. The probable effect of solution of pituitary on the recurrence of seizures as a result of its antidiuretic action is also suggested as in the previous experiments.

A boy, aged 15, had had grand mal attacks with increasing frequency for a period of two years, usually between midnight and 8 a. m. At the time of his admission for the present study, he was having from three to as many as twelve mild or moderately severe convulsions daily with only an occasional day of freedom. During the first eleven days after admission he was allowed to remain on the

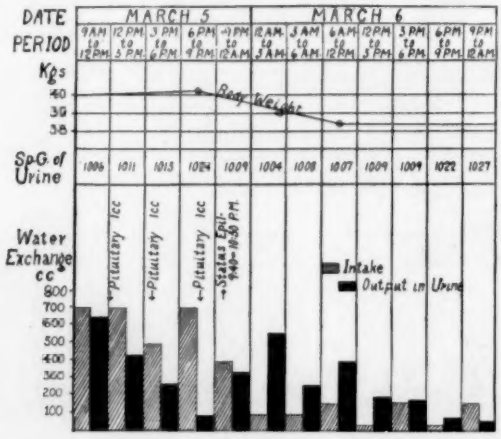

Chart 4.—Detailed analysis of that portion of chart 3 relating to the combined effect of solution of pituitary and excessive ingestion of water, three hour periods.

regular, relatively high carbohydrate, hospital diet while various acute diuresis and antidiuresis tests were made. It was modified slightly during the last half of this subperiod in such a way as to allow a considerable restriction of the fluid intake. During the second subperiod a borderline, nonketogenic, maintenance diet, containing a fairly limited amount of water, was given. For the third subperiod this same diet was supplemented with 15 Gm. of additional carbohydrate daily to insure against the occurrence of ketosis. It was observed, however, that occasional highly concentrated specimens of urine collected during the afternoon continued to give a faintly positive reaction to the ferric chloride test for aceto-acetic acid. This was probably due in large part to concentration of the normal amounts present, because quantitative determination of the twenty-four hour excretion of total acetone bodies showed no definite increase over the normal.

The chart shows clearly the contrast between the number of seizures occurring during periods of high water intake and that during periods of rather rigid restriction of water. It shows too that, at least in some

apparently severe epileptic cases, restriction of water alone may be very helpful in controlling seizures, even when a fair amount of leeway is given in the choice of the diet. Aside from the fact that the patient was emotionally upset on the twenty-seventh day at the prospect of losing his room-mate, we have found no definite reason for his having had a mild seizure on that day, for he remained free from attacks regularly thereafter as long as he adhered faithfully to the same regimen.

The last chart of the series, taken from the preceding one, is presented to show in greater detail what actually occurred during the period of six days which include the experiment involving the simultaneous forcing of water intake and administration of solution of pituitary at

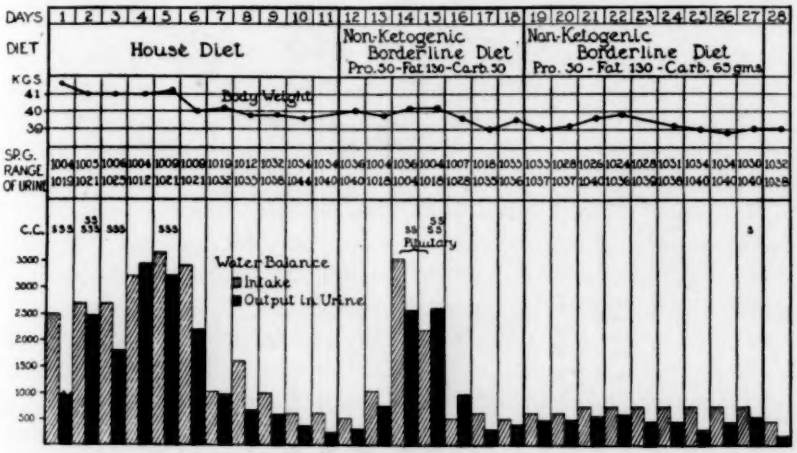

Chart 5.—Comparison of the effects of high and low intake of water, of different diets and of solution of pituitary on the occurrence of seizures (*S*) in J. B., a boy, aged 15 years.

sufficiently frequent intervals to force retention of fluid in the body. It is apparent that two seizures occurred in the first evening following a sudden increase in the intake of water on the same afternoon and twelve hours before the experiment with pituitary was begun, showing the effect of water alone. Whether the pituitary played a more important part than merely one of antidiuresis during the next period is not certain, but this interpretation is suggested by the fact that the seizures did not occur until two hours after the last of a series of injections, which resulted in definite retention of water. That these two series of seizures were directly related to the conditions of the experiment is practically certain from the fact that the first two occurred in the evening and the other four very close together near midday; whereas, practically, all of the patient's regular seizures occur in the early hours

of the morning and are usually far less severe than these. The chart shows that practically all of the excess water held in the body during this period was lost during the first twelve or fifteen hours following the seizures. This is shown by the large negative water balance and by the loss of body weight during this time.

GENERAL COMMENT

Such data as the foregoing, which are representative of a larger series of related observations made during the past two years strongly suggest a disturbance in the regulation of water exchange in the body in epilepsy. Most of the evidence points to the existence of an abnormal tendency

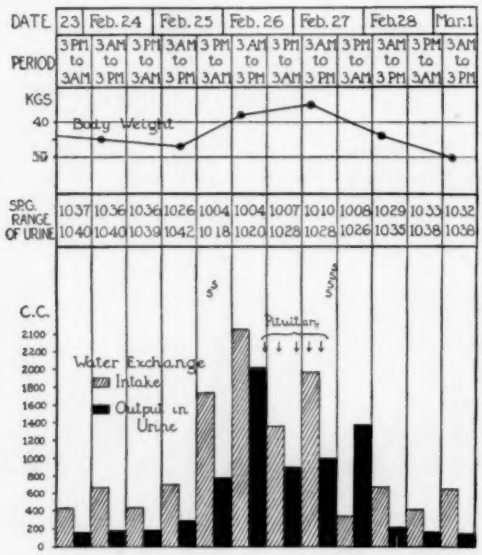

Chart 6.—Analysis of that period in chart 5 which deals with the effect of solution of pituitary plus increased ingestion of water, showing marked retention of water prior to seizures and marked diuresis after.

toward a positive water balance or to an unusual "sensitiveness" to changes in body water in this direction during the active phase of the disease and prior to the occurrence of seizures. The four different regimens which are known to favor the prevention of seizures, namely, fasting, a ketogenic diet, rigid restriction of fluid intake and the administration of large doses of acid-forming salts, have in common the effect of dehydrating the tissues. It is true that these four procedures likewise tend to maintain the hydrogen ion concentration of the body fluids at a slightly higher level than would otherwise exist, but all of the evidence so far obtained indicates that the relationship of any disturbance in acid-base equilibrium is of secondary importance as pointed out

in a previous report.[7] It can be said in a general way that, within rather wide limits, procedures which tend to cause a shift in the acid-base balance toward the acid side favor loss of body water, whereas those causing a shift in the opposite direction probably favor retention of water within the tissues. This intimate relationship of the acid-base balance and the water balance makes it difficult to ascertain which is of primary importance, so far as the occurrence of seizures is concerned.

The search for a crucial experiment that would aid in making this decision led us to determine the effect of the antidiuretic hormone of the pituitary gland during periods when water was restricted, as well as during periods when water was being given in excessive amounts. That administration of this hormone favors the occurrence of seizures under the conditions of our experiments seemed to us so nearly certain, after a number of cautious trials, that we considered it hardly justifiable to subject patients to further tests of the kind until a better antidote than we possess at present is available. That the antidiuretic action of the solution of pituitary used was responsible for the effects observed, and not the oxytocic action or the pressor action, is strongly suggested by the facts: first, that seizures tended to recur, not at the outset and immediately after single injections, but usually after a series of such injections and coincident with the enforced establishment of a positive water balance; and secondly, that the antidiuretic hormone alone, practically free from oxytocic principle, was even more effective than the solution of pituitary containing both substances. Although we have yet to study the effect of this hormone action on the acid-base equilibrium before drawing final conclusions, it appears probable that the pituitary extract acts by accentuating an abnormality already existing in one of the important mechanisms for regulating the water balance of the body or of the central nervous system and its membranes.

Some of the workers who have interested themselves in the problems of epilepsy, especially some of the neurosurgeons,[8] believe that all cases of the disease have a purely organic basis and that most of them sooner or later show evidence of accumulation of excessive amounts of water in the central nervous system, particularly in the subarachnoid spaces, where veritable reservoirs of cerebrospinal fluid may occur. Such authors usually assume that this abnormality is secondary to inflammatory, traumatic or congenital lesions, involving the absorption

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7. McQuarrie, Irvine; and Keith, H. M.: Experimental Study of the Acid-Base Equilibrium in Children with Idiopathic Epilepsy, Am. J. Dis. Child. **37**: 261 (Feb.) 1929.

8. Dandy, W. E.: The Space Compensating Function of the Cerebrospinal Fluid—Its Connections with Cerebral Lesions in Epilepsy, Bull. Johns Hopkins Hosp. **34**: 245, 1923. Dandy, W. E.: Impressions of the Pathology of Epilepsy from Operations, Am. J. Psychiat. **6**: 519, 1927.

paths of the cerebrospinal fluid. Undoubtedly there does exist such a group of patients and a small percentage of these are apparently cured or show improvement following surgical removal of obstructions to the outflow of the fluid. Such patients would probably respond favorably, at least for a short period of time, to the dehydration regimens used.[9]

The majority of investigators in the field, however, maintain that there is a very large group of noninstitutional young epileptic patients who show no primary structural changes whatsoever in the brain or its coverings. These authorities have long maintained that the underlying cause in such cases must be sought in abnormalities of function. Such opinions are supported not only by their inability to demonstrate primary lesions but by analogy with other convulsive conditions such as tetany, in which there is no organic lesion of the central nervous system but purely a metabolic disturbance affecting the rest of the body as well as the brain. What is greatly needed at the present time is further information regarding possible differentiation of types of epilepsy in children, particularly with reference to the aforementioned question. Fortunately, such data will probably be forthcoming from clinics such as that of Dr. Blackfan in Boston, where roentgen study of the central nervous system after injection of air into the partially evacuated subarachnoid space of children with unexplained convulsions has been almost a routine procedure during the past few years.

The exact nature of the relationship of water balance to the occurrence of seizures is as yet quite obscure. It may be that the beneficial effect of partial dehydration depends merely on the mechanical relief from excessive pressure within the fluid channels of the brain. This would seem to be the most likely explanation in those cases having abnormal accumulations of cerebrospinal fluid in the subarachnoid spaces due to organic obstructions which interfere with normal absorption. For the other type of case, however, in which no such structural changes are found, explanation for the facts observed must be sought in a possible disturbance in the physiologic regulation of water balance within the brain.

We are well aware that the data available at the present time do not justify the elaboration of an explanatory theory; but, we may state that one working hypothesis which has occurred to us is based on the possibility of an imbalance between naturally occurring extrarenal processes of diuresis (dehydration) and antidiuresis (hydration). An analogous imbalance is known to occur in the case of diabetes insipidus but in an opposite direction from that which we may postulate as being present in epilepsy.

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9. Although we could find no report in the literature regarding his work, we have recently heard through other persons that Dr. Fay of Philadelphia has experienced very satisfactory results merely from rigid restriction of fluids in such cases.

Among the various physiologic factors known to be concerned in the regulation of water balance in the tissues, the powerful antidiuretic or hydrating hormone which was recently isolated in practically pure form by Kamm and his co-workers [10] from the posterior lobe of the hypophysis cerebri might conceivably be responsible, if overactive, for a tendency on the part of the body to retain an excess of water. Such an effect might result, on the other hand, from underproduction of some normally-occurring, antagonistic, diuretic or dehydrating hormone such as that isolated by Bourquin [11] from the mammillary bodies and adjacent tissues of the brains of dogs suffering from experimental diabetes insipidus and from the same structures in other normal animals. In the event of hypo-activity, it would of course be unnecessary to assume more than normal activity on the part of the organ producing the antidiuretic principle, and this may conceivably be the situation in epilepsy. Altenberger and Stern [12] reported finding even a slight diminution in the oxytocic activity of the spinal fluid in half of the epileptic patients examined by them. They did not study the blood, nor did they test the pressor or melanophore-expansion activity of the spinal fluid, which would be the proper test for the antidiuretic hormone. Our own studies by means of the latter methods are as yet incomplete.

Although the relationship of such substances as hypophyseal extracts to the secretion by the choroid plexus of cerebrospinal fluid is still in dispute,[13] it is possible that such hormone antagonists as those mentioned may exert a profound regulating influence over the circulation of fluid in the brain and its membranes. In such an event it is even conceivable that the increase in cerebrospinal fluid and the brain "wetness," described in many of the old and severe cases of epilepsy, might be secondary to a long existing imbalance between the factors referred to and not necessarily the primary condition. The history of antecedent infection or trauma in itself hardly argues for one theory of epilepsy more than for another, because some kind of local injury either irritative or destructive may well be the starting point for the underlying abnormality of function.

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10. Kamm, Oliver; Aldrich, T. B.; Grote, I. W.; Rowe, L. W., and Bugbee, E. P.: The Active Principles of the Posterior Lobe of the Pituitary Gland, J. Am. Chem. Soc. **50**:573, 1928.

11. Bourquin, Helen: Studies on Diabetes Insipidus: II. The Diuretic Substance, Preliminary Observations, Am. J. Physiol. **83**: 125, 1927; Further Observations on the Diuretic Substance of Experimental Diabetes Insipidus, Proc. Am. Physiol. Soc., 1928, ibid **85**: 354, 1928.

12. Altenberger, H., and Stern, F.: Quantitative Estimation of Posterior Lobe Secretion in Cerebrospinal Fluid of Epileptics, Ztschr. f.d. ges. Neurol. u. Psychiat. **112**: 691, 1928.

13. Weed, L. H.: The Cerebrospinal Fluid, Physiol. Rev. **2**: 196 and 197, 1922.

Our tentative views regarding the possibility of disturbed water balance being closely identified with the etiologic factors in at least one group of epileptic subjects are now being tested in a variety of ways, such as that of determining the concentrations of the various naturally occurring diuretic and antidiuretic principles in the fluids of the body during different stages and phases of the disease. The therapeutic effect of such hormone-like diuretic preparations as may be obtained will be determined. Several other approaches to the problem are also being considered. We are convinced that no matter what the ultimate nature of the disorder may be, the degree of dysfunction varies greatly in different patients and in the same patient from time to time, for the severity of symptoms must parallel the degree of disturbance closely in this type of reaction.

We have observed in some of our epileptic subjects an accentuation of the normal tendency of the kidneys to excrete less water during sleep, particularly during the early morning hours, even when the rate of water intake has been uniform throughout the twenty-four hours. This may have some bearing on the increased frequency of seizures at this time of day.

The other convulsive disorders which seem to us to have seizure mechanisms most nearly resembling that in genuine epilepsy, as we are coming to view it, are experimental water intoxication as described by Larson, Weir and Rowntree [14] and eclampsia in pregnant women. As regards the latter condition, pituitary is said to be present in the body fluids in increased amounts during the latter part of pregnancy; there is undoubtedly a tendency for the eclamptic patient to develop an abnormal positive water balance; and the general clinical picture of eclampsia, as we have observed it, resembles that of epilepsy so closely during the acute convulsive stage that an oversupply of the antidiuretic principle (betahypophamine) seems highly probable as a contributing cause. It is hoped that we shall have the opportunity to test this possibility as a part of our present program of study of the convulsive diseases. If used by the preeclamptic patient, the dehydrating regimen subsequently described might prove to be a valuable prophylactic measure in this condition as it undoubtedly is in epilepsy.

COMMENT ON THE THERAPEUTIC ASPECTS OF THE LOW WATER EXCHANGE REGIMEN

Until the etiologic mechanisms of epilepsy and allied convulsive disorders are better understood and natural specific remedial agents or operative procedures are available, it will be necessary to continue our

14. Larson, E. E.; Weir, J. F., and Rowntree, L. G.: Studies in Diabetes Insipidus, Water Balance and Water Intoxication, Arch. Int. Med. **29**: 306 (March) 1922.

search for improvements in the therapeutic regimens that we have at our disposal. The method which we have found to be most suitable for the routine management of the epileptic child differs from the ketogenic dietary regimen already in vogue in that emphasis is placed primarily on the establishment of water balance at a much reduced level. We believe that the effectiveness of fasting and the ketogenic diet is due not so much to the presence of ketosis per se as to the associated dehydrating effect.

When attention is concentrated solely on the amounts of carbohydrate, protein and fat contained in the diet, patients with severe epilepsy are frequently encountered who continue to have seizures in spite of marked ketosis. Such a result is most common, for instance, when water is being given ad libitum and the carbohydrate allowed is selected largely from the so-called 3 to 10 per cent vegetables and fruits, which possess an alkaline ash and contain 90 per cent or more of water. In a case such as this, however, if the intake of water is considerably restricted and any cereal grain product is substituted for the watery green vegetables or fruits to supply the carbohydrate allowed, seizures will usually cease to occur. Of course, it is desirable to vary the dietary somewhat, and it is essential for it to contain all of the vitamins in required amounts. Some of the leafy vegetables and oranges are, therefore, included, but their water and alkali, as well as their carbohydrate contents, must be taken into account and limitations made according to the severity of the patient's symptoms and other conditions. Fresh yeast or yeast extract has been used when the allowance of green vegetables has needed to be greatly limited.

When a patient with severe epilepsy comes under treatment, the seizures may be brought under control by fasting and somewhat stringent restriction of water or by giving nothing but 2 cc. of 30 per cent cream per kilogram of body weight every four hours during the day for a period of from two to five days. A trial maintenance diet, containing protein, fat and carbohydrate in such proportions as to keep the patient near the borderline of ketosis, is then given for a number of days, the allowance of carbohydrate being made up largely from relatively concentrated cereal grain products, such as bread. The water is restricted as far as possible without causing the patient too great discomfort. The thirst usually complained of at first is often satisfactorily alleviated by allowing the patient to chew a small piece of gum, paraffin or soft rubber.

From this point on it is simply necessary by the method of trial and error to adjust the regimen to the optimum levels of water intake and ketogenesis compatible with both the physiologic requirements of the body, including growth, and the prevention of seizures. For the severe case fairly rigid restriction of both water and carbohydrate may be necessary at first for control of seizures, but in the less severe cases the

restriction of water may need to be only moderate, if the diet is kept just above the threshold of ketosis. Until we have made further studies of the water metabolism of children under various conditions, we cannot say what the minimum water requirement of the body is, but some of our patients are apparently doing satisfactorily on a total intake of between 15 and 30 cc. per kilogram of body weight daily, including that in their food, as estimated from standard food tables. During initial periods of dehydration in the severe cases, we have used far less than this amount for a few days, as shown in the charts.

We have found (unpublished data) that the amount of protein required by growing children on strongly ketogenic diets is nearer to 2 Gm. per kilogram of body weight than to the 1 Gm. allowance that we and various other observers had formerly assumed to be adequate. The less strongly ketogenic the diet, of course, the lower is the protein requirement. In diets only slightly above the threshold of ketosis, at least 1 Gm. per kilogram should be given. The effect of the restriction of water per se on the protein requirement is not known, but it is probably only slight.

Two important reasons for preferring to employ a combination of restriction of water and the borderline diet as against the ketogenic diet alone are, first, that the latter tends to be accompanied by a negative calcium and phosphorus balance, as shown by Nelson,[15] and, secondly, that a rather marked hypercholesterinemia has been found to follow its use in some of our cases (unpublished data). The ultimate effect of this may be deleterious as claimed by Joslin.[16]

Further experience may demonstrate the value of some natural and relatively harmless diuretic as an adjunct to this form of therapy, but we have not made crucial tests regarding such a possibility up to the present time. It is likely also that other procedures, which cause loss of body water, such as saline catharsis, will be found to aid in the control of acute outbursts, but this again remains for future testing.

SUMMARY AND CONCLUSIONS

The superficial relationship between water balance and the occurrence of seizures has been determined under various conditions in a number of epileptic children.

There appears to be a tendency for the epileptic subject to retain water during the active phase of the disease in amounts which are harmful. Convulsions tend to occur when a positive water balance above a certain magnitude is established. When diuresis follows the seizure, it

15. Nelson, M. V.: Calcium and Phosphorus Metabolism of Epileptic Children Receiving a Ketogenic Diet, Am. J. Dis. Child. **36**:716 (Oct.) 1928.

16. Joslin, E. P.: Arteriosclerosis and Diabetes, Ann. Clin. Med. **5**:1061, 1927.

favors the prevention of further seizures temporarily. Whether this effect of the extra water is due solely to changes within the brain cannot be said as yet.

Procedures, such as fasting, the use of ketogenic diets and stringent restriction of water with nonketogenic, borderline diets, lead to partial dehydration of the tissues and prevention of seizures. Suddenly increasing the intake of water during the course of treatment by dehydration tends to cause recurrence of seizures, at least in the severe cases.

Parenteral administration of solution of pituitary,[17] or of the antidiuretic hormone of hypophysis, causes the development of a positive water balance and the occurrence of seizures in the epileptic subject. Urea in large doses causes loss of the retained water.

Possible underlying etiologic factors in the disease are discussed in the light of these observations. A disturbance in water balance, perhaps affecting the central nervous system more specifically, appears to be closely identified with the etiology of epilepsy.

The general principles of a rational therapeutic regimen based on experimental data and clinical experience are outlined.

Additional work in progress is outlined.

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17. Dr. Oliver Kamm of the Research Laboratory of Parke, Davis and Company supplied us with the pituitary solution.

METABOLISM OF UNDERNOURISHED CHILDREN

VIII. THE EFFECT OF HIGH AND LOW PROTEIN DIETS ON THE EXCRETION OF CREATINE, CREATININE AND AMMONIA *

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AND
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During the course of our study on the effect of high and low protein diets on the nitrogen and caloric balance of undernourished children, determinations of the creatine, creatinine and ammonia outputs have also been made. A perusal of the literature revealed that no similar studies on undernourished children have been reported.

EXPERIMENTAL WORK

Forty experiments of a minimum of three days each were conducted on eight normal and ten underweight children between the ages of 4 and 12 years. All but three of the children were girls.

The high protein diet consisted of approximately 4 Gm. of protein per kilogram of body weight and included about 50 Gm. of meat daily, the rest of the protein being supplied by milk and eggs. The low protein diet was low only by comparison, since it contained about 2 Gm. of protein per kilogram of body weight, which is considered a safe allowance for children of the age studied. The protein of this diet was derived chiefly from milk and eggs, exclusive of meat.

In each case, the diet was continued over a period of at least six days, the feces and twenty-four hour specimens of urine being collected during the last three days. The total intake and the total output of nitrogen, together with the urinary output of creatine, creatinine and ammonia were determined by analysis, according to methods described in one of our previous papers.[1] In some cases the high protein diet preceded the low protein diet, and no interval was allowed between the two diets, while in others the order reversed, and an interval of several days or even weeks elapsed.

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1. Wang, C. C.; Frank, M.; Kern, R., and Hays, B. B.: Metabolism of Undernourished Children: III. Urinary Nitrogen with Special Reference to Creatinine, Am. J. Dis. Child. **32**:360 (Sept.) 1926.

Average values for three day periods on each diet are given in tables 1, 2 and 3.

TABLE 1.—*Influence of High and Low Protein Diets on the Excretion of Creatine and Creatinine*

Subject	Age	Sex	Weight: Found, Kg.	Weight: Deviation from Normal, per Cent	Nitrogen Intake: Per 24 Hours, Gm.	Nitrogen Intake: Per Kg. per 24 Hours, Gm.	Creatine as Creatinine: Per 24 Hours, Mg.	Creatine as Creatinine: Per Kg. per 24 Hours, Mg.	Ratio: Creatine N × 100 / Total N Output	Creatinine: Per 24 Hours, Mg.	Creatinine: Per Kg. per 24 Hours, Mg.	Coefficient
HIGH PROTEIN DIET												
Normal												
R. W.	11	F	35.3	+8.0	15.4	0.44	453	12.8	1.5	598	16.9	6.3
A. Ge.	5	F	17.9	+0.6	12.2	0.68	305	17.1	1.4	266	14.8	5.5
H. P.	4	F	17.4	+0.6	11.8	0.68	374	21.5	1.6	201	11.5	4.3
S. W.	8	F	21.9	—1.4	13.9	0.63	329	15.0	1.3	444	20.3	7.6
B. L.	11	F	31.3	—1.6	13.8	0.44	496	15.9	1.6	639	20.4	7.6
F. J.	10	F	27.5	—2.5	13.9	0.50	502	18.2	1.6	565	20.5	7.6
R. G.	10	F	27.9	—3.1	13.8	0.49	333	11.9	1.1	514	18.4	6.8
K. B.	8	F	20.7	—3.7	12.1	0.59	376	18.2	1.4	391	18.9	7.0
Aver.	8.4		25.0	—0.4	13.4	0.56	396	16.3	1.4	452	17.3	6.6
Underweight												
W. K.	12	M	28.6	—5.3	18.0	0.63	537	18.8	1.4	626	21.9	8.1
G. C.	10	M	26.9	—5.3	17.8	0.66	582	21.6	1.5	675	25.1	9.3
A. Go.	10	F	27.6	—6.1	14.0	0.51	490	17.8	1.5	603	21.9	8.0
H. K.	10	M	21.7	—8.8	13.7	0.63	454	20.9	1.6	469	21.6	8.0
K. Be.	8	F	20.6	—10.5	13.5	0.65	398	19.3	1.5	337	16.4	6.1
E. S.	4	F	13.7	—11.0	9.1	0.67	251	18.3	1.2	191	13.9	5.2
F. B.	10	F	17.8	—13.2	10.4	0.58	353	19.8	1.3	344	19.3	7.2
L. B.	11	F	25.8	—17.8	16.5	0.64	491	18.5	1.6	431	16.7	6.2
A. B.	6	F	16.9	—18.0	9.6	0.56	258	15.3	1.4	271	16.1	6.0
A. G.	10	F	22.8	—23.4	14.0	0.61	399	17.5	1.4	448	19.6	7.3
A. G.	10	F	20.6	—26.3	13.7	0.67	316	15.3	1.4	397	19.3	7.2
Aver.	9.2		22.1	—13.2	13.7	0.62	412	18.5	1.4	436	19.3	7.1
LOW PROTEIN DIET												
Normal												
R. W.	11	F	34.7	+6.1	7.3	0.21	183	5.3	1.1	556	16.0	6.0
A. Ge.	5	F	17.1	—1.2	5.9	0.34	167	9.8	1.4	250	14.6	5.4
S. W.	8	F	21.0	—2.8	6.4	0.31	138	6.5	1.0	434	20.6	7.7
B. L.	11	F	30.9	—2.8	6.2	0.21	201	6.5	1.3	651	21.1	7.8
H. P.	4	F	16.5	—2.9	4.8	0.29	191	11.6	1.6	186	11.3	4.2
F. J.	10	F	26.9	—4.6	6.7	9.25	158	5.9	1.1	532	19.8	7.4
K. B.	8	F	20.5	—4.7	6.3	0.31	156	7.6	1.1	375	18.1	6.8
R. G.	10	F	22.1	—5.9	6.6	0.24	116	4.3	0.8	507	18.7	7.0
Aver.	8.4		24.3	—2.3	6.3	0.27	164	7.2	1.2	436	17.5	6.5
Underweight												
W. K.	12	M	28.5	—5.6	9.9	0.35	250	8.8	1.3	615	21.6	8.0
A. G.	10	F	27.5	—6.5	6.6	0.24	200	7.3	1.3	599	21.8	8.1
G. C.	10	M	26.0	—7.5	9.2	0.35	214	8.2	1.3	592	22.8	8.5
H. K.	10	M	21.6	—9.3	7.1	0.33	178	8.2	1.1	456	21.1	7.8
A. B.	6	F	18.6	—11.0	5.0	0.27	141	7.6	1.0	313	16.8	6.2
K. Be.	8	F	20.2	—12.2	6.0	0.30	160	7.9	1.3	337	16.7	6.2
F. B.	10	F	17.5	—14.7	5.3	0.32	147	8.4	1.2	315	18.0	6.7
E. S.	4	F	12.7	—15.9	5.1	0.40	119	9.2	1.1	162	12.8	4.7
M. D.	7	F	18.5	—16.3	5.6	0.30	160	8.6	1.1	358	19.4	7.2
L. B.	11	F	25.1	—20.1	7.4	0.29	180	7.2	1.2	456	18.2	6.8
A. B.	6	F	16.4	—20.4	5.5	0.33	121	7.4	1.4	271	16.5	6.1
A. G.	10	F	22.0	—23.3	5.5	0.25	165	9.5	1.5	442	20.1	7.5
A. G.	10	F	20.1	—23.6	5.7	0.28	157	7.8	1.3	396	19.7	7.3
Aver.	8.8		21.1	—14.3	6.5	0.21	167	8.2	1.2	409	18.9	7.0

RESULTS

Excretion of Creatine.—All of the children, on both high and low protein diets, regardless of age or sex, excreted creatine. The average output expressed as creatinine per kilogram of body weight was slightly

TABLE 2.—*Influence of Age on the Excretion of Creatine and Creatinine*

Subject	Age	Sex	Percentage Variation from Normal Weight	Nitrogen Intake per Kg., Gm.	Creatine as Creatinine per Kg., Mg.	Ratio: Creatine N × 100 / Total N Output	Creatinine: Per Kg., Mg.	Creatinine: Coefficient
HIGH PHOTEIN DIET								
H. P.	4	F	+ 0.6	0.68	21.5	1.6	11.5	4.3
E. S.	4	F	−11.0	0.67	18.3	1.2	13.9	5.2
A. Ge.	5	F	+ 0.6	0.68	17.1	1.4	14.8	5.5
A. B.	6	F	−18.0	0.56	15.3	1.4	16.1	6.0
Average	5		− 4.0	0.65	18.1	1.4	14.1	5.3
S. W.	8	F	− 1.4	0.63	15.0	1.3	20.3	7.6
K. B.	8	F	− 3.7	0.59	18.2	1.4	18.9	7.0
K. Bo.	8	F	−10.5	0.65	19.3	1.5	16.4	6.1
F. J.	10	F	− 2.5	0.50	18.2	1.6	20.5	7.6
R. G.	10	F	− 3.1	0.49	11.9	1.1	18.4	6.8
G. C.	10	M	− 5.3	0.66	21.6	1.5	25.1	9.3
A. Go.	10	F	− 6.1	0.51	17.8	1.5	21.9	8.0
H. K.	10	M	− 8.8	0.63	20.9	1.6	21.6	8.0
F. B.	10	F	−13.2	0.58	19.8	1.3	19.3	7.2
A. G.	10	F	−23.4	0.61	17.5	1.4	19.6	7.3
A. G.	10	F	−26.3	0.67	15.3	1.4	19.3	7.2
Average	10		− 9.5	0.59	17.8	1.4	20.1	7.5
R. W.	11	F	+ 8.0	0.44	12.8	1.5	16.9	6.3
B. L.	11	F	− 1.6	0.44	15.9	1.6	20.4	7.6
L. B.	11	F	−17.8	0.64	18.5	1.6	16.7	6.2
W. F.	12	M	− 5.3	0.63	18.8	1.4	21.9	8.1
Average	11		− 4.2	0.54	16.5	1.5	19.0	7.1
LOW PROTEIN DIET								
H. P.	4	F	− 2.9	0.29	11.6	1.6	11.3	4.2
E. S.	4	F	−15.9	0.40	9.2	1.1	12.8	4.7
A. Ge.	5	F	− 1.2	0.34	9.8	1.4	14.6	5.4
A. B.	6	F	−11.0	0.27	7.6	1.0	16.8	6.2
A. B.	6	F	−20.4	0.33	7.4	1.4	16.5	6.1
Average	5		−10.3	0.33	9.1	1.3	14.4	5.3
M. D.	7	F	−16.3	0.30	8.6	1.1	19.4	7.2
S. W.	8	F	− 2.8	0.31	6.5	1.0	20.6	7.7
K. B.	8	F	− 4.7	0.31	7.6	1.1	18.1	6.8
K. B.	8	F	−12.2	0.30	7.9	1.3	16.7	6.2
F. J.	10	F	− 4.6	0.25	5.9	1.1	19.8	7.4
R. G.	10	F	− 5.9	0.24	4.3	0.8	18.7	7.0
A. G.	10	F	− 6.5	0.24	7.3	1.3	21.8	8.1
G. C.	10	M	− 7.5	0.35	8.2	1.3	22.8	8.5
H. K.	10	M	− 9.3	0.33	8.2	1.1	21.1	7.8
F. B.	10	F	−14.7	0.32	8.4	1.2	18.0	6.7
A. G.	10	F	−23.3	0.25	9.5	1.5	20.1	7.5
A. G.	10	F	−23.6	0.28	7.8	1.3	19.7	7.3
Average	9		−11.0	0.29	7.5	1.2	19.7	7.4
R. W.	11	F	+ 6.1	0.21	5.3	1.1	16.0	6.0
B. L.	11	F	− 2.8	0.21	6.5	1.3	21.1	7.8
L. B.	11	F	−20.1	0.29	7.2	1.2	18.2	6.8
W. K.	12	M	− 5.6	0.35	8.8	1.3	21.6	8.0
Average	11		− 5.6	0.27	7.0	1.2	19.2	7.2

higher on both diets in the children in the underweight group than in those in the normal group. The protein intake, however, caused much more striking differences in the creatine output than the degree of underweight. In the case of the normal children the creatine output,

expressed as creatinine per kilogram of body weight amounted to 16.3 mg. on the high protein diet and 7.2 mg. on the low. For the undernourished children, the figures were 18.5 and 8.2. In spite of the wide variation in the nitrogen intake and the creatine output, if the total

TABLE 3.—*Influence of High and Low Protein Diets on Excretion of Ammonia*

Subject	Age	Sex	Weight: Found, Kg.	Weight: Deviation from Normal, per Cent	Nitrogen Intake: Per 24 Hours, Gm.	Nitrogen Intake: Per Kg. per 24 Hours, Gm.	Nitrogen Output: Per 24 Hours, Gm.	Nitrogen Output: Per Kg. per 24 Hours, Gm.	Ammonium Nitrogen: Per 24 Hours, Mg.	Ammonium Nitrogen: Per Kg. per 24 Hours, Mg.	Ammonium Nitrogen: Total Nitrogen, per Cent
HIGH PROTEIN DIET											
Normal											
R. W.	11	F	35.3	+8.0	15.4	0.44	11.4	0.32	470	13.3	4.1
A. Ge.	5	F	17.9	+0.6	12.2	0.68	7.9	0.44	268	14.9	3.4
H. P.	4	F	17.4	+0.6	11.8	0.68	8.9	0.51	290	16.7	3.3
S. W.	8	F	21.9	−1.4	13.9	0.63	9.4	0.43	284	12.9	3.0
B. L.	11	F	31.3	−1.6	13.8	0.44	11.9	0.38	430	13.7	3.6
F. J.	10	F	27.5	−2.5	13.9	0.50	11.5	0.42	383	13.9	3.3
R. G.	10	F	27.9	−3.1	13.8	0.49	10.9	0.39	449	16.1	4.1
K. B.	8	F	20.7	−3.7	12.1	0.59	10.0	0.48	250	12.5	2.6
Aver.	8.4		25.0	−0.4	13.4	0.56	10.2	0.42	354	14.3	3.4
Underweight											
W. K.	12	M	28.6	−5.3	18.0	0.63	14.2	0.50	482	16.7	3.4
G. C.	10	M	26.9	−5.3	17.8	0.66	14.2	0.53	365	13.6	2.6
A. Go.	10	M	27.6	−6.1	14.0	0.51	12.3	0.44	568	20.6	4.6
H. K.	10	M	21.7	−8.8	13.7	0.63	10.7	0.50	435	20.1	4.1
K. Bo.	8	F	20.6	−10.5	13.5	0.65	9.7	0.47	294	14.3	3.0
E. S.	4	F	13.7	−11.0	9.1	0.67	8.0	0.58	224	16.4	2.8
F. B.	10	F	17.8	−13.2	10.4	0.58	9.3	0.52	264	14.8	2.8
L. B.	11	F	25.8	−17.8	16.5	0.64	11.3	0.44	206	10.3	2.4
A. B.	6	F	16.9	−18.0	9.6	0.56	6.9	0.41	293	17.4	4.3
A. G.	10	F	20.6	−23.4	13.7	0.67	8.4	0.41	368	17.9	4.4
A. G.	10	F	22.8	−26.3	14.0	0.61	10.4	0.46	417	18.3	4.0
Aver.	9.2		22.1	−13.2	13.7	0.62	10.5	0.48	361	16.4	3.5
LOW PROTEIN DIET											
Normal											
R. W.	11	F	34.7	+6.1	7.1	0.21	6.6	0.19	314	9.1	4.8
A. Ge.	5	F	17.1	−1.2	5.9	0.34	4.4	0.25	230	13.5	5.3
S. W.	8	F	21.0	−2.8	6.4	0.31	5.2	0.25	206	9.8	4.0
B. L.	11	F	30.9	−2.8	6.2	0.21	5.9	0.20	318	10.3	5.4
H. P.	4	F	16.5	−2.9	4.8	0.29	4.4	0.27	207	12.5	4.7
F. J.	10	F	26.9	−4.6	6.7	0.25	5.5	0.20	252	9.4	4.6
K. B.	8	F	20.5	−4.7	6.3	0.31	5.2	0.26	215	10.5	4.1
Aver.	8.1		23.9	−1.8	6.2	0.27	5.0	0.23	249	10.7	4.7
Underweight											
W. K.	12	M	28.5	−5.6	9.9	0.36	6.8	0.24	311	10.9	4.6
R. G.	10	F	27.1	−5.9	6.6	0.24	5.3	0.19	256	9.4	4.9
A. G.	10	F	27.5	−6.5	6.6	0.24	5.7	0.21	349	12.7	6.2
G. C.	10	M	26.0	−7.5	9.2	0.35	7.7	0.30	308	11.9	4.0
H. K.	10	M	21.6	−9.3	7.1	0.33	6.0	0.28	252	11.7	4.2
A. B.	6	F	18.6	−11.0	5.0	0.27	4.1	0.22	252	13.5	6.2
K. B.	8	F	20.2	−12.2	6.0	0.30	4.5	0.22	225	11.1	5.0
F. B.	10	F	17.5	−14.7	5.5	0.32	4.6	0.26	200	11.4	4.4
E. S.	4	F	12.7	−15.9	5.0	0.41	4.1	0.32	160	12.6	4.0
M. D.	7	F	18.5	−16.3	5.6	0.30	5.2	0.28	231	12.5	4.4
L. B.	11	F	25.1	−20.1	7.4	0.30	5.6	0.22	228	9.1	4.1
A. B.	6	F	16.4	−20.4	5.5	0.33	3.2	0.20	209	12.7	6.7
A. G.	10	F	20.1	−23.3	5.7	0.28	4.2	0.21	259	12.9	6.1
A. G.	10	F	22.0	−23.6	5.5	0.25	4.5	0.20	265	12.0	5.9
Aver.	8.9		21.2	−13.7	6.5	0.31	5.1	0.24	250	11.7	5.1

grams of creatine nitrogen excreted are computed as a coefficient of the total nitrogen output, a fairly constant relationship is found between the two, the ratio $\frac{\text{creatine N}}{\text{total N output}} \times 100$ showing an average of 1.4 for both normal and undernourished children on the high protein diet and of

1.2 for both groups on the low protein diet. Thus it appears that the creatine output parallels closely the nitrogen output and therefore the nitrogen intake.

Creatinine.—The creatinine output computed per kilogram of body weight was also slightly higher on both diets in the undernourished group than in the normal group. It is, however, less marked than creatine. The difference in the excretion of creatinine is most likely due to the age difference of the two groups. Unlike the creatine the amount of protein in the diet had little influence on the excretion of creatinine. The average values expressed as creatinine nitrogen per kilogram of body weight for the normal group was 6.6 mg. on the high protein diet and 6.5 mg. on the low protein diet. The corresponding figures for the undernourished group were 7.1 and 7.

Excretion of Creatine and Creatinine According to Age.—In table 2 is given the creatine and creatinine output of our subjects arranged according to age. This table shows that the creatine output tends to decrease slightly and that the creatinine output tends to increase slightly with the age of the child. These results are in accordance with those reported by other investigators,[2] although the increase in creatinine output is not so marked as has been noted in some instances.

It should be pointed out that the decrease in the creatine output is accompanied by a decrease in the nitrogen intake per kilogram of body weight. The question may be raised, therefore, whether this decrease in urinary creatine is due to a similar decrease in nitrogen intake or whether it is due, as has been previously assumed, to an increased ability of the older child to metabolize this substance. It is possible that both of these factors come into play in determining the total creatine output.

Excretion of Ammonia.—The ammonia excreted by both normal and undernourished children was higher per kilogram of body weight, but formed a lower percentage of the total nitrogen output on the high protein diet than on the low protein diet. On both diets the undernourished children excreted somewhat larger quantities of ammonia than the well nourished. Our results here agree with those of Utheim,[3] and of some earlier investigators quoted by her, who found a high excretion of ammonia in athreptic infants.

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2. Rose, W. C.: Excretion of Creatine in Infancy and Childhood, J. Biol. Chem. **10**:265, 1911-1912. Harding, V. J., and Gaebler, O. H.: The Influence of the Positive Nitrogen Balance upon Creatinuria during Growth, ibid. **57**:25 (Aug.) 1923; On the Constancy of the Creatine-Creatinine Excretion in Children on a High Protein Diet, ibid. **54**:579 (Nov.) 1922.

3. Utheim, K.: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances (Athrepsia), Am. J. Dis. Child. **22**:329 (Oct.) 1921.

COMMENT

The slight increase in creatine output when computed per kilogram of body weight in the undernourished group is probably due to the corresponding increase in the protein intake as well as to the comparatively greater proportion of active tissue in the bodies of these children since the total output on fairly constant nitrogen intake is fairly constant. On the other hand, creatinine excretion is apparently independent of the quantity of the proteins in the diet, provided that the latter is chiefly

TABLE 4.—*Influence of Protein Intake on the Excretion of Creatine and Creatinine (Denis and Kramer)*

Subject	Protein Intake, per Kg. per 24 Hours, Gm.	Creatine Excretion		Creatinine Excretion			Total Creatinine Coefficient
		Per 24 Hours, Mg.	Per Kg. per 24 Hours, Mg.	Per 24 Hours, Mg.	Per Kg. per 24 Hours, Mg.	N. Per Kg. per 24 Hours, Mg.	
1, Girl	2.60	180	15.0	140	11.7	4.4	295
5 years	2.34	146	12.2	131	10.9	4.1	257
12 Kg.	2.08	173	14.4	152	12.7	4.7	301
	1.67	113	9.4	137	11.4	4.2	235
	1.51	105	8.8	142	11.7	4.4	233
	0.57	71	5.9	143	11.9	4.4	204
	0.73	42	3.5	133	11.1	4.1	169
2, Boy	2.56	132	7.7	200	11.7	4.4	314
6 years	1.06	101	5.9	199	11.6	4.3	286
17.1 Kg.	0.88	77	4.5	189	11.1	4.1	256
	0.99	41	2.4	189	11.1	4.1	224
	0.80	26	1.5	190	11.1	4.1	212
	0.66	18	1.1	191	11.2	4.2	207
	0.51	9	0.5	206	12.0	4.5	214
	0.44	3	0.2	213	12.5	4.7	216
	0.40	4	0.2	211	12.3	4.6	214
	0.95	73	4.3	219	12.8	4.8	282
	1.58	88	5.2	217	12.7	4.7	293
	1.91	105	6.1	210	12.3	4.6	301
3, Boy	2.23	60	3.7	190	11.7	4.4	242
6 years,	1.42	122	7.5	210	12.9	4.8	315
4 months	0.92	16	1.0	223	13.7	5.1	237
16.25 Kg.	0.69	3	0.2	196	12.1	4.5	199
	0.77	0	...	210	12.9	4.8	210
	1.15	114	7.0	230	14.2	5.3	329
	1.58	121	7.5	215	13.2	4.9	320
	1.92	152	9.4	219	13.5	5.0	354
4, Boy	1.88	170	10.0	200	11.8	4.4	348
5 years	1.58	223	13.1	190	11.2	4.2	384
17 Kg.	1.10	130	7.6	210	12.4	4.6	323
	0.77	20	1.2	220	12.9	4.8	237
	0.66	6	0.4	204	12.0	4.5	209

derived from milk. The difference in the age of the two groups and the difference in the proportion of active tissue in the body probably account for the higher value of this compound found in the undernourished group.

According to Utheim,[3] the higher ammonia output per kilogram of body weight is probably due to the greater demand for alkali to neutralize the excessive fatty acids produced in the intestines and eliminated as soaps in the undernourished children. The loss of alkali in the tissues is made up by the ammonia formed in the body and excreted in the urine.

In comparing our data with those of other investigators on the study of the excretion of creatine and creatinine in children, we find that we agree well with the results of Denis and Kramer,[4] who reported that the excretion of creatine in four children between 5 and 6 years of age and one infant observed by them ran parallel to the nitrogen intake and that the creatine could be made to disappear altogether from the urine when the nitrogen intake was sufficiently low. These investigators also report a constant total excretion of creatinine. When this is recomputed (table 4) on the basis of kilograms of body weight, these figures are somewhat lower than those observed by us.

Since our high protein diet contained a small amount of meat, our figures are not strictly comparable with those of Harding and Gaebler [5] who concluded that normal children of the same age and under the same environment excrete the same quantity of total creatine (creatinine and creatine in terms of creatine), and that if the total creatine in milligrams is expressed as a coefficient of the body weight in kilograms, the figure obtained is a constant, independent of the age of the child, and is of the same magnitude as the creatinine coefficient of an adult man.

Our figures for the excretion of both creatine and creatinine are consistently higher than those of the aforementioned authors and do not seem to us to support so definite a conclusion regarding the reciprocal relationship between creatine and creatinine metabolism in children. The discrepancy between our results and those of Harding and Gaebler, however, may be due to differences in the creatine content of the diet used, due to the presence of some meat and perhaps to the inclusion of larger amounts of milk.

CONCLUSIONS

1. The excretion of creatine, creatinine and ammonia of undernourished children per kilogram of body weight is slightly higher than that of children of normal weight. This is probably due in part to a larger proportion of muscular tissue in the bodies of the underweight children.

The higher creatine output is undoubtedly due in part to the slight increase computed per kilogram of body weight of protein intake in the undernourished children. The slight increase in the excretion of creatinine is probably due to the difference in age in the two groups, since this compound is independent of protein intake. The increased production and excretion of organic acid in the undernourished children may account for the higher excretion of ammonia.

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4. Denis, W., and Kramer, J. G.: Influence of Protein Intake on Creatine Excretion in Children, J. Biol. Chem. **30**:189, 1917.

5. Harding and Gaebler (footnote 2, third reference).

2. The creatine output of both normal and underweight children is directly proportional to the nitrogen intake.

3. The ratio $\frac{\text{creatine N}}{\text{total N output}} \times 100$ is fairly constant. Hence, there is constant relationship between protein intake and creatine output.

4. The creatinine output in such children is dependent on body weight and is independent of protein intake. It is, therefore, constant when computed per kilogram of body weight.

5. No abnormality in the elimination of the waste products, creatine, creatinine and ammonia was found in undernourished children.

METABOLISM OF UNDERNOURISHED CHILDREN

IX. A STUDY OF THE BASAL METABOLISM, CALORIC BALANCE AND PROTEIN METABOLISM DURING A PERIOD OF GAIN IN WEIGHT *

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In the previous papers of this series, average results obtained from the observations of groups of different children of varying degrees of undernourishment have been reported. Since the constitution of normal people is known to vary to a certain extent in different persons, the slight difference in metabolic processes reported in our previous papers might be attributed to individual difference rather than to the variations in the degree of undernourishment. In this communication we therefore present the results of studies of the basal metabolism, caloric balance and protein metabolism of the same children at different stages of their approach to normal weight. The children remained at the hospital for several months or until their weight became within 10 per cent of the average for their age and height. Twelve children were studied, nine of them being used for the protein study, nine for the study of basal metabolism and six for the study of caloric exchange. Five of the children were observed in all three studies. The technic used in these studies was that described in former papers.[1]

So far as we have been able to discover, no similar studies on undernourished children have been reported in the literature.

BASAL METABOLISM

Our observations on the same children at varying degrees of underweight coincide closely with those already reported on different children.[2]

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1. Wang, C. C.; Frank, M.; Hays, B. B., and Kern, R.: Metabolism of Undernourished Children: I. Gain in Weight, Am. J. Dis. Child. **32**:63 (July) 1926; II. Basal Metabolism, ibid. **32**:350 (Sept.) 1926. Wang, C. C.; Hawks, J. E., and Hays, B. B.: V. Protein Metabolism, ibid. **35**:968 (June) 1928. Wang, C. C.; Kaucher, M., and Frank, M.: VI. Caloric Balance, ibid. **36**:979 (Nov.) 1928.

2. Wang and others (footnote 1, second reference).

The basal metabolism of the nine children observed was within normal limits at all degrees of underweight. In most cases, however, when computed per kilogram of body weight, there was a decided decrease in the basal metabolism as the child gained. With one exception, R. G., the basal metabolism per square meter of body surface also decreased, provided the height remained the same. In this one case, the child could not be kept perfectly still, so that the figures given probably do not represent a true basal metabolic rate.

In a few cases, the pulse rate seemed to decrease as the child gained in weight. In most cases, however, the pulse rate remained about the

TABLE 1.—*Influence of Gaining in Body Weight on Basal Metabolism*

			Weight		Height				Heat Production						
						Variation from Average									
Subject	Age	Sex	Found, Kg.	Variation from Standard, per Cent	Found, Cm.	Baldwin Standard, per Cent	Boas Standard, per Cent	Surface Area, Sq. M.	Stem Length, Cm.	Per 24 Hours, Calories	Per Kg. per Hour, Calories	Per Square Meter per Hour, Calories	Pulse Rate	Respiratory Quotient	Activity
A. Go.	10	F	20.9	−25.9	132	− 3.6	+0.8	0.906	71	921	44	42.4	92	0.81	−
A. Go.	8	F	18.0	−25.3	125	− 1.6	+3.3	0.812	68	784	44	40.2	88	0.77	−
A. Go.	10	F	23.0	−20.0	133	− 2.9	+1.5	0.942	72	1013	44	44.8	88	0.80	+
A. Go.	10	F	26.6	− 9.5	134	− 2.2	+2.3	1.010	72	1082	41	44.6	88	0.79	−
A. Go.	10	F	27.5	− 6.5	134	− 2.2	+2.3	1.024	72	1011	37	41.1	82	0.82	−
S. K.	10	M	25.6	−16.1	137	± 0.0	+3.8	0.984	74	1086	42	46.0	80	0.79	−
S. K.	10	M	27.6	− 9.5	137	± 0.0	+3.8	1.006	74	1055	38	41.2	78	0.79	−
A. B.	6	F	17.0	−14.8	116	+ 1.8	+5.5	0.757	63	882	52	48.5	86	0.80	+
A. B.	6	F	18.9	− 9.6	117	+ 2.6	+6.4	0.790	64	889	47	46.9	88	0.80	+
L. C.	6	F	17.2	−14.0	115	+ 0.9	+4.5	0.751	63	931	54	51.7	94	0.85	−
L. C.	6	F	18.0	−11.3	115	+ 0.9	+4.5	0.766	63	904	50	49.2	94	0.86	+
L. C.	6	F	18.5	− 8.9	115	+ 0.9	+4.5	0.774	63	868	47	46.7	100	0.85	−
B. G.	8	F	19.4	−12.2	120	− 5.5	−0.8	0.814	65	980	50	50.2	94	0.81	+
B. G.	9	F	20.5	− 6.7	121	− 8.3	−4.0	0.838	66	938	46	46.6	84	0.86	+
N. G.	7	M	15.3	−10.5	106	−13.1	−9.4	0.673	58	1052	69	65.1	86	0.79	++
N. G.	7	M	16.8	− 1.8	106	−13.1	−9.4	0.758	58	862	51	47.4	84	0.79	−
R. G.	6	M	16.4	− 7.3	108	− 7.7	−3.6	0.703	60	960	59	57.3	88	0.85	++
R. G.	6	M	16.9	− 4.5	108	− 7.7	−3.6	0.712	59	999	59	58.5	82	0.84	++
J. G.	8	M	22.1	− 5.9	123	− 3.2	−0.8	0.877	63	1117	51	53.1	92	0.84	+
J. G.	8	M	22.6	− 5.0	124	− 2.4	+1.6	0.890	64	1123	50	52.6	90	0.83	+
E. G.	6	F	17.0	− 4.5	108	− 5.3	−1.8	0.714	59	984	56	57.4	84	0.81	−
E. G.	6	F	18.1	− 0.5	109	− 4.4	−0.9	0.738	60	976	54	55.1	86	0.81	+

same. The respiratory quotient also was almost constant for individual children.

CALORIC BALANCE

In this study, also, the results for the same children agree closely with those for different children at varying degrees of underweight.[3] The calories utilized per kilogram of body weight depend on the caloric intake per kilogram of body weight and were entirely independent of the degree of undernutrition or of the weight of the feces, as Fleming [4]

3. Wang and others (footnote 1, fourth reference).

4. Fleming, G. B., and Hutchison, H. S.: A Study of the Metabolism in the Undernourished Infant, Quart. J. Med. **17**:339 (July) 1923.

reported. The percentage utilization was normal in all cases, and remained practically constant as the child gained in weight. These results support the conclusions drawn in a previous communication,[3] namely that the absorptive power of children of the degree of underweight studied by us is equal to that of the normal child.

PROTEIN METABOLISM

Again the results of our studies on the same children confirm the observations for different children at different stages of underweight.

TABLE 2.—*Influence of Gaining in Body Weight on Caloric Balance*

Name	Sex	Age	Weight		Intake	Output per Kilogram			Utilization		
			Found, Kg.	Deviation from Normal Weight, per Cent	24 Hours, Cals.	Per Kg., Cals.	Urine, Cals.	Feces, Cals.	Total Cals.	Per Kg., Cals.	Per Cent	Feces, Per Kg. Cals.
E. F.	F	6	15.2	—16.5	1680	110.5	3.4	6.5	9.9	100.6	91.0	1.29
			15.4	—13.5	1243	80.7	3.4	4.2	7.5	73.2	90.7	0.59
			17.3	— 4.9	1798	103.9	3.6	4.6	8.2	95.7	92.1	0.88
			19.3	+ 4.9	1713	88.8	3.0	4.4	7.4	81.4	91.7	0.88
S. K.	M	10	25.4	—16.7	2312	91.0	3.0	5.6	8.6	82.4	90.5	1.17
			26.8	—12.1	2349	87.7	2.7	4.4	7.1	80.5	91.9	0.96
			27.5	— 9.8	2307	83.9	3.0	4.2	7.2	76.7	91.4	0.90
N. G.	M	7	15.0	—12.3	1673	111.5	3.6	5.4	9.0	102.5	91.9	1.07
			16.5	— 3.5	1553	94.1	3.0	5.7	8.7	85.4	90.7	1.52
			16.9	— 1.2	1556	92.1	2.7	3.7	6.4	85.6	93.0	0.79
E. G.	F	6	16.3	— 8.4	1147	70.4	2.7	3.3	6.0	64.4	91.5	0.63
			17.5	— 1.7	1620	92.6	2.5	5.5	8.0	84.6	91.4	1.14
			17.5	— 1.7	1653	94.5	3.0	3.0	6.0	88.5	93.7	0.86
			18.1	— 1.1	1628	89.9	2.9	5.3	8.2	81.8	91.0	1.02
B. G.	F	8	19.1	—13.6	2081	108.9	3.5	4.6	8.1	100.8	92.6	0.95
			20.5	— 8.5	1705	83.2	3.5	4.9	8.4	74.8	89.9	0.70
L. C.	F	6	17.1	—15.8	1309	76.6	2.3	4.6	6.9	69.7	91.0	1.37
			18.0	—11.3	1604	89.1	2.5	4.9	7.4	81.7	91.7	0.99
			18.4	— 9.4	1721	93.5	2.8	5.6	8.4	85.2	91.1	1.21
			18.7	— 7.9	1691	90.4	2.6	6.8	9.4	81.1	93.4	1.33

The percentage absorption of nitrogen is practically constant for each child. The absorption per kilogram of body weight varies with the intake, the absorption being lower when the intake is lower. Since the total protein intake was approximately the same for each child, the intake per kilogram of body weight and the absorption per kilogram of body weight tended to decrease slightly as the child gained in weight.

The retention of nitrogen decreased markedly in all cases, both per kilogram of body weight and per centum, as the child gained in weight. This fact constitutes further evidence for the conclusion that the undernourished child has been undergoing a period of protein starvation, due probably to a low protein intake, and needs a more liberal protein allowance than the normal child.

TABLE 3.—*Influence of Gaining in Body Weight on Nitrogen Metabolism*

			Weight		Intake		Output						Absorption			Retention		
							Urine		Feces		Total							
Name	Sex	Age	Found, Kg.	Variation from Normal, per Cent	24 Hrs., Gm.	Per Kg., Gm.	24 Hrs., Gm.	Per Kg., Gm.	24 Hrs., Gm.	Per Kg., Gm.	24 Hrs., Gm.	Per Kg., Gm.	24 Hrs. Gm.	Per Kg., Gm.	Per Cent of Intake	24 Hrs., Gm.	Per Kg., Gm.	Per Cent of Intake
E. F.	F	6	15.2	—16.5	9.2	0.605	6.1	0.401	0.89	0.059	7.0	0.461	8.3	0.546	90.2	2.2	0.145	23.9
			15.4	—13.5	9.2	0.597	6.6	0.429	0.70	0.045	7.3	0.474	8.5	0.552	92.4	1.9	0.123	20.7
			17.3	— 4.9	9.9	0.572	7.7	0.445	1.06	0.061	8.8	0.509	8.8	0.509	88.9	1.1	0.064	11.1
			19.3	+ 4.9	10.0	0.518	8.0	0.415	0.89	0.046	8.9	0.461	9.1	0.472	91.0	1.1	0.057	11.0
E. G.	F	6	16.3	— 8.4	9.5	0.583	6.4	0.393	1.00	0.061	7.4	0.454	8.5	0.521	89.5	2.1	0.129	22.1
			17.5	— 1.7	8.7	0.497	5.9	0.337	0.79	0.045	6.7	0.383	7.9	0.451	90.8	2.0	0.114	23.0
			17.5	— 1.7	8.8	0.503	6.3	0.360	0.87	0.050	7.2	0.411	7.9	0.451	89.8	1.6	0.091	18.2
			18.1	— 1.1	8.9	0.492	6.8	0.376	0.81	0.045	7.6	0.420	8.1	0.448	91.0	1.3	0.072	14.6
N. G.	M	7	15.0	—12.3	10.3	0.687	7.0	0.467	0.96	0.064	8.0	0.533	9.3	0.620	90.3	2.3	0.153	22.3
			16.5	— 3.5	9.7	0.588	6.5	0.394	0.86	0.052	7.4	0.449	8.8	0.533	90.7	2.3	0.139	23.7
			16.9	— 1.2	9.8	0.580	7.5	0.444	0.90	0.053	8.4	0.497	8.9	0.527	90.8	1.4	0.083	14.3
L. C.	F	6	17.1	—15.8	8.4	0.491	5.0	0.292	0.65	0.038	5.7	0.333	7.7	0.450	91.6	2.7	0.158	32.1
			18.0	—11.3	9.4	0.522	6.6	0.367	0.69	0.038	7.3	0.406	8.7	0.483	92.6	2.1	0.117	22.3
			18.4	— 9.4	9.1	0.496	6.7	0.364	0.68	0.037	7.4	0.402	8.4	0.457	92.3	1.7	0.092	18.7
			18.7	— 6.5	9.3	0.497	7.0	0.374	0.72	0.039	7.7	0.412	8.6	0.460	92.5	1.6	0.086	17.2
S. K.	M	10	25.4	—16.7	15.3	0.602	11.9	0.469	1.01	0.040	12.9	0.508	14.3	0.563	93.5	2.4	0.094	15.7
			26.8	—12.1	15.9	0.593	12.3	0.459	1.10	0.041	13.4	0.500	14.8	0.552	93.1	2.5	0.093	15.7
			27.5	— 9.8	14.5	0.527	11.4	0.415	1.07	0.039	12.5	0.455	13.4	0.487	92.4	2.0	0.073	13.8
A. G.	F	8	17.9	—25.7	10.6	0.592	6.6	0.369	1.00	0.056	7.6	0.425	9.6	0.536	90.6	3.0	0.168	28.3
A. G.	F	10	20.6	—25.9	13.7	0.665	8.4	0.408	1.10	0.053	9.5	0.461	12.6	0.612	91.8	4.2	0.204	30.7
			26.6	— 9.5	13.0	0.489	8.9	0.335	1.10	0.041	10.0	0.376	11.9	0.447	91.5	3.0	0.113	23.1
			27.6	— 6.1	11.0	0.399	8.7	0.315	0.93	0.034	9.6	0.348	10.1	0.368	91.8	1.4	0.051	12.7
B. B.	F	5	11.2	—19.3	7.4	0.661	4.8	0.429	0.64	0.057	5.4	0.482	6.8	0.607	91.9	2.0	0.179	27.0
			12.0	—11.8	8.2	0.683	5.8	0.483	0.77	0.064	6.6	0.550	7.4	0.617	90.2	1.6	0.133	19.5
B. G.	F	8	19.1	—13.6	10.0	0.523	5.8	0.304	1.05	0.055	6.8	0.356	8.9	0.468	89.5	3.2	0.166	31.6
B. G.	F	9	20.5	— 8.5	10.5	0.512	7.7	0.376	0.70	0.034	8.4	0.410	9.8	0.478	93.3	2.1	0.102	20.0
H. D.	M	5	13.2	— 9.4	7.0	0.530	5.1	0.386	0.60	0.045	5.7	0.432	6.4	0.485	91.4	1.3	0.098	18.6
			13.8	— 0.0	7.9	0.573	5.9	0.428	0.80	0.058	6.7	0.486	7.1	0.515	89.9	1.2	0.087	15.2

SUMMARY

The basal metabolism, the caloric exchange and the nitrogen metabolism of twelve undernourished children were studied at intervals as they were gaining in weight.

The results confirm our observations on different children of varying degrees of underweight; namely, (1) that the basal metabolism of undernourished children is apparently normal, (*2*) that the absorptive power of undernourished children is equal to that of normal children and (*3*) that the retention of nitrogen in undernourished children is greater than that in children of normal weight, and as these children approach normal weight the retention of nitrogen decreases.

RICKETS IN CHICKS

IV. THE EFFECT OF HEAT AND EXPOSURE TO AIR ON THE STABILITY OF VITAMIN D*

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Cod liver oil is the richest natural source of two vitamins which play an important part in the diet of both human beings and animals, vitamins A and D. That the former is readily destroyed by oxidation, through exposure to air, is generally accepted, but in spite of evidence to the contrary it is still believed by many people, particularly by those dealing with the utilization of cod liver oil, that vitamin D cannot be destroyed by exposure to air or that it is so extremely resistant to such oxidation that the question of destruction by exposure to air need be given no consideration.

It seems probable that this conception of the stability of vitamin D has arisen from the fact that this vitamin was distinguished from vitamin A through a difference in the relative rate of oxidation when heated and exposed to air. As early as 1921, Mellanby [1] reported: "Butter, heated and oxidized for four hours, loses some antirachitic action. Cod liver oil similarly treated still has strong antirachitic effect." This statement does not imply that vitamin D cannot be destroyed by oxidation but suggests rather the opposite conclusion.

In 1922, McCollum, Simmonds and Becker [2] presented a paper on "An Experimental Demonstration of the Existence of a Vitamin Which Promotes Calcium Deposition." These authors stated in this paper: "We have shown experimentally that cod liver oil oxidized for twelve to twenty hours does not cure xerophthalmia in rats. It does, however, cause deposition of calcium in the bones of young rats suffering from rickets. This shows that oxidation destroys fat-soluble A without destroying another substance which plays an important rôle in bone growth."

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* From the Laboratory of Poultry Nutrition, Cornell University Agricultural Experiment Station.

1. Mellanby, E.: Experimental Rickets, Medical Research Council, Special Report Series, 1921, no. 61.

2. McCollum, E. V.; Simmonds, Nina, and Becker, J. Ernestine: Studies on Experimental Rickets: XXI. An Experimental Demonstration of the Existence of a Vitamin Which Promotes Calcium Deposition, J. Biol. Chem. **53**:293, 1922.

This may be taken as a positive statement that vitamin D cannot be destroyed by the method of oxidation employed, although it is not believed that this was so intended. Moreover, this conclusion cannot be drawn from the data presented. The oxidized cod liver oil was fed, in every instance, at a level of 2 per cent of the diet. Yet it was shown that the untreated oil produced beginning healing of rickets when included in the diet to the extent of 0.6 per cent. At least 70 per cent of the D vitamin content of the oil, when fed at the 2 per cent level, could have been destroyed, and still enough would have been unoxidized to equal that in untreated oil fed at a level of 0.6 per cent. Had the oxidized cod liver oil also been fed at this level, it is probable that some destruction of vitamin D would have been demonstrated.

In 1923, Steenbock and Nelson [3] and Steenbock, Hart, Jones and Black [4] presented evidence which confirmed the discovery of vitamin D by McCollum, Simmonds and Becker. Aerated cod liver oil was also used in these studies. Steenbock and Nelson, however, did not conduct their work on the basis of the complete resistance of vitamin D to destruction by aeration. In the report of their work they stated: "For our experimental work we selected material treated for twenty hours, as we surmised that after forty hours of aeration the antirachitic as well as the antiophthalmic property might have been destroyed, because we know from the experience of Hart, Steenbock, Hoppert, Bethke and Humphrey [5] that the antirachitic factor is not a stable quantity."

In the work by Steenbock, Hart, Jones and Black, the same cod liver oil was used that had been aerated for twenty hours by Steenbock and Nelson. It was not demonstrated that the D vitamin was completely resistant to oxidation by aeration.

Goldblatt and Zilva [6] also presented evidence, in 1923, in confirmation of the conclusions of McCollum, Simmonds and Becker in respect to the separate entity of the antirachitic factor. Their experimental work, however, was conducted in such a manner as to determine approximately the minimum protective dosage of the untreated as well

3. Steenbock, H., and Nelson, E. M.: Fat-Soluble Vitamin: XIII. Light in Its Relation to Ophthalmia and Growth, J. Biol. Chem. **56**:355, 1923.

4. Steenbock, H.; Hart, E. B.; Jones, J. H., and Black, A.: Fat-Soluble Vitamins: XIV. The Inorganic Phosphorus and Calcium of the Blood Used as Criteria in the Demonstration of the Existence of a Specific Antirachitic Vitamin, J. Biol. Chem. **58**:59, 1923-1924.

5. Hart, E. B.; Steenbock, H.; Hoppert, C. A.; Bethke, R. M., and Humphrey, G. C.: Dietary Factors Influencing Calcium Assimilation: III. The Comparative Efficiency of Timothy Hay, Alfalfa Hay, and Timothy Hay Plus Calcium Phosphate (Steamed Bone Meal) in Maintaining Calcium and Phosphorus Equilibrium in Milking Cows, J. Biol. Chem. **54**:75, 1922.

6. Goldblatt, H., and Zilva, S. S.: The Relation Between the Growth-Promoting and Antirachitic Functions of Certain Substances, Lancet **2**:647, 1923.

as of the aerated cod liver oil in respect to both the A and the D vitamins or, as they called them, the antirachitic and the growth-promoting functions. From the data obtained, Goldblatt and Zilva concluded that "the growth-promoting and antirachitic properties of cod liver oil are inactivated at different rates by heat in the presence of air." Furthermore, data were presented which showed that after aerating the cod liver oil for twenty-four hours at 120 C. no evidence of the antirachitic function was obtained when a daily dosage of 450 mg. was given.

In view of the fact that the results of Goldblatt and Zilva have been either overlooked or disregarded in many instances, it seemed desirable to obtain further evidence concerning the resistance of the D vitamin of cod liver oil to oxidation. Experiments of this nature, therefore, were started during the summer of 1925 with chicks as the experimental animal.

EXPERIMENTAL PROCEDURE

The cod liver oil used in these experiments was a medicinal oil of Norwegian origin. Its vitamin D potency had been previously determined with chicks by the use of a preventive technic. When fed at a level of 0.5 per cent of the ration, it was found to prevent or nearly prevent the development of rickets and to give normal growth until 8 weeks of age. The minimum protective dosage of this particular cod liver oil was therefore about 0.5 per cent. In view of this fact, the oil was fed at a level of 0.5 per cent in this series of experiments.

EXPERIMENT 1.—In the first experiment a supply of the oil was oxidized for twelve, twenty-four and forty-eight hours respectively by passing carbon dioxide-free, moisture-free air into it. The oil was maintained at the temperature of boiling water by means of a water-bath, and the air was heated to this temperature before entering the oil by conducting it through a coil immersed in boiling water.

Five lots of chicks were used. These were designated as lots 1, 2, 3, 4 and 5. Lot 1 received 0.5 per cent of untreated cod liver oil; lot 2, 0.5 per cent of cod liver oil that had been oxidized for twelve hours; lot 3, 0.5 per cent of cod liver oil that had been oxidized for twenty-four hours, and lot 4, 0.5 per cent of cod liver oil that had been oxidized for forty-eight hours. Lot 5 served as a rachitic control and received no cod liver oil.

The basal ration used was one known to give normal growth and normal bone development either when an adequate amount of vitamin D was included in it or when sufficient exposure to unfiltered sunshine was given. The cod liver oil was fed in the basal ration.

Each lot contained forty white leghorn chicks of our own strain. These chicks were first weighed when 48 hours old, and weekly thereafter. The experiment was conducted for a period of six weeks.

When the chicks were weighed, observations were made as to the development of rickets. No chick was considered rachitic unless it showed actual stiffness of gait and lameness, even though swelling of the hock, an indication of beginning rickets, had been previously observed.

The results of this experiment are given in chart 1. The chicks in lot 1 showed no evidence of rickets throughout the experimental

period and developed at a rate in excess of the normal growth of white leghorns, according to the data of Card and Kirkpatrick.[7]

The chicks in lot 2 showed evidence of the development of rachitic lameness at 6 weeks of age. At this time, 2.8 per cent of the chicks were actually lame. The final average weight was 69 Gm. less than that of lot 1.

Lot 3 showed definite evidence of rickets when the chicks were 3 weeks old. At this time, 2.5 per cent of the chicks were lame. This condition increased until at 6 weeks of age 60 per cent of the entire lot were rachitic. The average weight at the end of the period of growth was 58 Gm. less than that of the preceding lot.

In lot 4, 7.5 per cent of the chicks were lame at 3 weeks of age, and at 6 weeks all were rachitic. Growth development was 52 Gm. less than in lot 3.

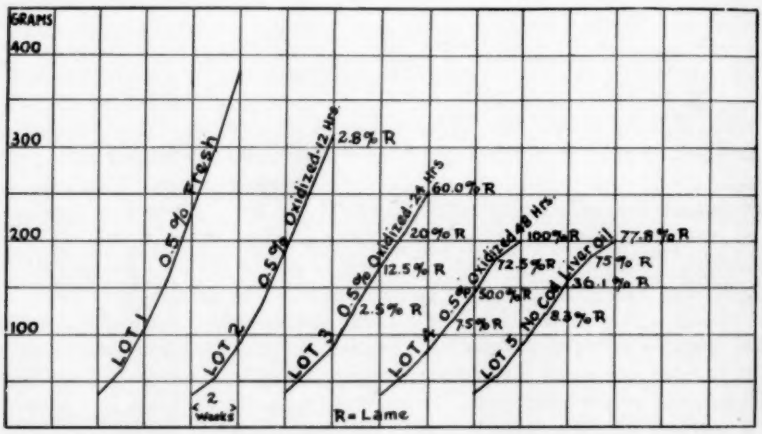

Chart 1 (experiment 1).—Rate of growth and percentage of rachitic lameness.

Lameness also developed in the control lot at 3 weeks of age, involving 8.3 per cent of the chicks. This increased rapidly until at six weeks, 77.8 per cent were definitely rachitic. For some unknown reason, although at 5 weeks of age the percentage of lameness in the control lot was slightly in excess of that in lot 4, the number of cases of rickets during the sixth week did not develop proportionately. If lameness only is used as a measure, the chicks in the control lot appeared, at the end, in better condition than those in lot 4. The final average weight, however, was the same in both these lots at the conclusion of the experiment. Since a deficiency in vitamin D affects growth, it

7. Card, L. E., and Kirkpatrick, W. F.: Rearing Chickens: Part I. Normal Rate of Growth in White Leghorns and Rhode Island Reds, Connecticut (Storrs) Agricultural Experiment Station, 1918, bull. 96, p. 355.

is more probable that the rachitic condition of the chicks in these lots was approximately the same.

The results of this experiment indicate some destruction of vitamin D by exposing heated cod liver oil to a stream of air for twelve hours; material destruction occurs at twenty-four hours' exposure and complete destruction at forty-eight hours'. When compared with lot 5, the rachitic control, neither growth nor occurrence of rachitic lameness shows that the chicks in lot 4 received any benefit from the addition of 0.5 per cent of cod liver oil that had been oxidized for forty-eight hours.

EXPERIMENT 2.—In the second experiment, the cod liver oil used was taken from the same supply as that of the preceding experiment. Oxidation was conducted in a similar manner and quantities of oil were oxidized for twelve and twenty-four hours, respectively.

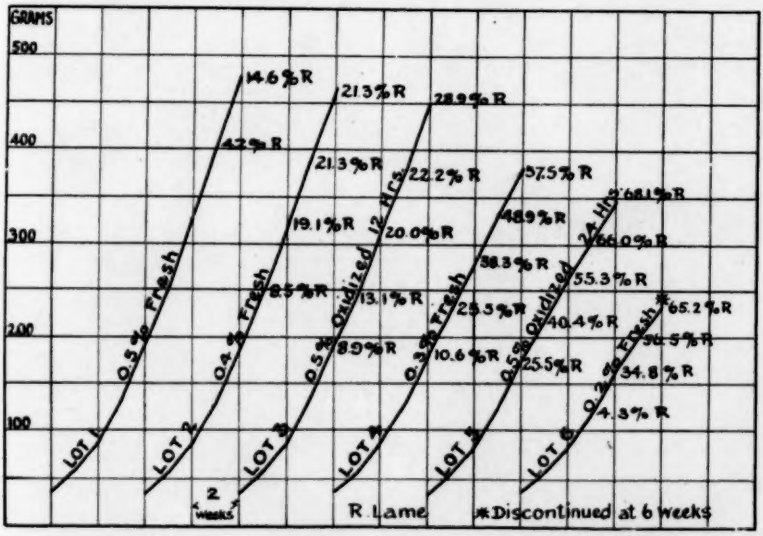

Chart 2 (experiment 2).—Rate of growth and percentage of rachitic lameness.

The period of growth in this experiment was increased to eight weeks. Untreated cod liver oil was fed not only at a level of 0.5 per cent, but also at levels of 0.4 per cent, 0.3 per cent and 0.2 per cent. These were lots 1, 2, 4 and 6, respectively. The chicks in lot 3 were given 0.5 per cent of cod liver oil, oxidized for twelve hours; those in lot 5 received 0.5 per cent of cod liver oil, oxidized for twenty-four hours. One lot in which no cod liver oil was given was not included in this experiment.

Each lot contained fifty white leghorn chicks. They were given the same basal ration and were managed in the same manner as those in the first experiment.

The rate of growth obtained in this experiment and the occurrence of rachitic lameness are presented in chart 2. Lot 1 developed at an approximately normal rate; at 8 weeks of age, their final average

weight was only slightly below normal. Evidence of rickets, however, developed at 7 weeks, and at 8 weeks 14.6 per cent of the chicks were rachitic. Lameness, while definitely evident, was not severe.

In lot 2, 8.5 per cent of the chicks were lame at 5 weeks of age. This condition increased slowly so that at 8 weeks only 21.3 per cent were rachitic. Final growth was only slightly less than that in lot 1.

Rickets developed, at the age of 4 weeks, in the chicks in lot 3 which received cod liver oil oxidized for twelve hours. Lameness occurred two weeks earlier than in the same lot in experiment 1. The increase, however, was gradual; at 8 weeks of age, only 28.9 per cent of the chicks were lame. The incidence of rickets at 6 weeks of age was greater than that in the corresponding lot of the first experiment. The average weight at 6 weeks of age was 315 Gm., which approximately equaled that of the same lot in the preceding experiment.

This difference in the development of rickets is probably due to a difference in storage of the vitamin D in the chicks used in the two experiments. The chicks of the first experiment were hatched in early summer so that the parent stock had full opportunity to recover from any possible deficiency in sunlight caused by the preceding winter season. On the other hand, the chicks in the second experiment were hatched during January. In this case the parent stock may have had insufficient exposure to sunlight, as November and December are the stormiest periods of the year at this latitude. Insufficient exposure to sunlight would result in a smaller storage of vitamin D in the eggs, as has been pointed out by Bethke, Kennard and Sassaman.[8]

Rickets developed in the chicks in lot 4 at 4 weeks of age and increased more rapidly than in the preceding lots. At 8 weeks of age, 57.5 per cent of the chicks were definitely rachitic. Whereas final growth in the preceding lots did not vary more than 27 Gm., the final average weight of this lot was from 70 to 97 Gm. less.

Among the chicks in lot 5, which received cod liver oil oxidized for twenty-four hours, the incidence of rickets was rather large at 4 weeks of age and increased rapidly to 68.1 per cent at 8 weeks. The development of rickets was slightly less at 6 weeks of age than in the same lot of the preceding experiment, and the average weight at 6 weeks was 16 Gm. greater.

Lameness developed in the chicks in lot 6 which received 0.2 per cent of untreated cod liver oil at 3 weeks of age. At 6 weeks, 65.2 per cent were lame. Severe rickets had developed in so many of these that experiments on this lot were discontinued.

8. Bethke, R. M.; Kennard, D. C., and Sassaman, H. L.: The Fat-Soluble Vitamin Content of Hens' Eggs as Affected by the Ration and Management of the Layers, J. Biol. Chem. **72**:695, 1927.

At 8 weeks of age, lots 1 and 5 were tested for analysis of bones. Only male chicks were selected for this purpose, to avoid any possibility of variation in skeletal development due to sex difference.

Before selection, these were divided into three groups according to degree of lameness. The groups were designated as normal, lame and very lame. Those put in the normal group showed no evidence of lameness; those in the lame group showed definite evidence of lameness or

Ash, Calcium and Phosphorus in Left Femur and Tibia of Male Chicks at 8 Weeks of Age, Together with Percentage of Rachitic Lameness, Final Weight and Severity of Rib Beading

Description of Lot With Total Number of Male Chicks	Final Grouping with Number of Male Chicks	Rachitic Lameness, per Cent	Number of Male Chicks	Weight at 8 Weeks	Rib Beading	Ash in Femur and Tibia, Gm.	Ash in Fat-Free Dry Bone, per Cent	Calcium in Fat-Free Dry Bone, per Cent	Phosphorus in Fat-Free Dry Bone, per Cent
Lot 1: 0.5 per cent fresh cod liver oil (24 male chicks)	Normal (20)	0.0	368	520	—	1.4204	43.06	15.99	7.82
			371	525	—	1.4890	46.06	17.10	8.45
			383	540	—	1.4029	44.20	16.47	8.02
			Average	528		1.4374	44.44	16.52	8.10
	Lame (4)	16.7	367	420	+	1.2466	39.36	14.22	7.08
			376	395	+	1.0286	39.05	13.88	7.20
			395	310	++	0.9698	36.77	13.22	6.65
			Average	375		1.0783	38.86	13.77	6.98
	All males	16.7	...	499		1.3776*	43.43*	16.06*	7.91*
Lot 5: 0.5 per cent cod liver oil, oxidized for 24 hours (25 male chicks)	Normal (7)	0.0	602	390	+	0.9602	38.56	13.63	8.45
			606	500	—	1.2497	42.56	15.14	7.84
			644	480	+	1.2029	41.78	15.08	7.50
			Average	457		1.1376	40.97	14.62	7.93
	Lame (8)	32.0	615	370	+	0.9270	38.42	13.61	7.05
			627	355	+++	0.9148	36.97	12.96	6.71
			629	380	+++	1.1542	40.48	13.89	7.43
			Average	368		0.9987	38.62	13.49	7.06
	Very lame (10)	40.0	611	255	++	0.6897	37.97	13.63	6.76
			639	265	+++	0.5088	35.61	11.54	6.42
			640	250	++++	0.6065	36.76	12.90	6.54
			Average	257		0.6017	36.78	12.69	6.57
	All males	72.0	...	360		0.8787*	38.54*	13.49*	7.11*

* These data are calculated by multiplying the averaged analytic data of each group in each lot by the number of chicks in the group, adding the results together and dividing by the total number of chicks per lot.

stiffness of gait and those in the last group were so lame that they could scarcely walk. There were no birds in lot 1 which could be included in the last mentioned group. In lot 1 there were twenty normal chicks and four lame ones, while in lot 5 there were seven normal, eight lame and ten very lame ones.

Three male chicks were taken from each group for analysis of bones. Selection was so made that the average weight of the birds chosen approximately equaled the average weight of the male chicks of their respective group.

The left tibia and left femur were removed from each of these birds and were analyzed for bone ash, calcium and phosphorus.

The results of these analyses are presented in the accompanying table, together with data showing the percentage of rachitic lameness, the weight of the male chicks selected and the beading of the ribs at the juncture with the spinal column.

COMMENT

These results show that the birds selected from the normal group, lot 1, were approximately normal in respect to ash, calcium and phosphorus content of leg bones, for male fowl chicks of this age, fed the particular type of basal ration used.[9]

The ash, calcium and phosphorus content of the leg bones of the lame group, lot 1, were significantly lower than that in the preceding group. Some beading of the ribs was obtained in this group but none in the normal group.

The birds of the normal group, lot 5, did not have as much ash, calcium and phosphorus in the leg bones as the normal birds in lot 1. Two of the three birds showed evidence of beading of the ribs.

The analytic results, however, for the lame group of lot 5 were nearly the same as for the lame group of lot 1, but beading of the ribs was more severe.

In the very lame group, lot 5, the lowering of the ash, calcium and phosphorus content of the bones of the legs was significantly greater than that in the preceding group, and beading of the ribs was more severe.

The probable amount of ash, calcium and phosphorus in the bones of the legs for the average male chick of each lot was calculated. The data were obtained by multiplying the average analytic data of each group in each lot by the number of chicks in the group, adding the results and dividing by the total number of chicks per lot.

Perhaps too much reliance should not be placed on this procedure. Yet it is interesting to note in this connection that the results of the analysis of the bones of the legs of all the male chicks in lot 4, obtained for other experimental purposes, support this calculation. The average ash content of the bones of the legs of all the male chicks of this lot was 1.0911 Gm.; the precentage of ash was 39.61, the percentage of calcium 14.39 and the percentage of phosphorus 7.14. These values are only slightly greater than the calculated averages for the chicks in lot 5 that had received cod liver oil oxidized for twenty-four hours.

9. Heuser, G. F., and Norris, L. C.: Rickets in Chicks: III. The Effectiveness of Mid-Summer Sunshine and Irradiation from a Quartz Mercury Vapor Arc in Preventing Rickets in Chicks, Poultry Science **8**:89, 1929.

This corresponds to the incidence of rachitic lameness in lot 4 which was slightly less than that in lot 5, and the rate of growth, which was somewhat greater. It is felt, therefore, that such a calculation of the probable analysis of the average male chick in lots 1 and 5 is justified and serves to give a clearer picture of the relative bone development.

In this experiment, as in the preceding one, both the results of growth and the occurrence of rachitic lameness indicate some destruction of vitamin D of cod liver oil after oxidation for twelve hours, and material destruction after oxidation for twenty-four hours. This conclusion is supported, furthermore, by observations on beading of the ribs and analysis of the bones of the legs of male chicks from lots 1 and 5. The increase in severity of beading of the ribs and the marked reduction of the ash, calcium and phosphorus content in the bones of the legs of the male chicks in lot 5 cannot be explained except on the basis of destruction of vitamin D in the cod liver oil used.

SUMMARY

1. In this work, rate of growth, development of rachitic lameness, beading of the ribs and determination of the ash, calcium and phosphorus in the bones of the legs of white leghorn chicks are used as a means of determining the resistance of vitamin D of cod liver oil to oxidation at the temperature of boiling water by means of carbon dioxide-free, moisture-free air.

2. The results indicate that vitamin D is not a stable vitamin when heated and exposed to air, and substantiate in this respect the conclusions of Goldblatt and Zilva.

BLOOD CHOLESTEROL IN DIABETIC CHILDREN*

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Considerable diversity of opinion exists among workers as to what constitutes the normal range of value of the blood cholesterol in children. Gordon and Cohn [1] studied the plasma cholesterol in normal children of different ages. They obtained figures varying from 110 to 170 mg. per hundred cubic centimeters of plasma. Baranski [2] determined the blood cholesterol in ninety-five children and found it always within the normal adult range. Goldbloom and Gottlieb [3] found values for whole blood between 175 and 200 mg. per hundred cubic centimeters in a number of normal children. One worker, de Toni,[4] found higher average values in children than in adults. The latter observer, however, reported higher values for calcium and sugar in the young, an observation not corroborated by other workers.

My own observations would lead one to believe that the normal range of values is greater in children than in adults, owing to the larger number of low figures obtained. Bloor's [5] method was used, and the determinations were made on the plasma unless otherwise indicated. Because of their rarity in normal persons, I have regarded values in excess of 200 mg. per hundred cubic centimeters as indicative of hypercholesteremia.

The literature contains further differences of opinion as to the frequency with which patients with diabetes have abnormal values for blood cholesterol. Denis [6] found hypercholesteremia in only a few cases of diabetes and considered its determination of no clinical value. Bang [7] found increases in serum cholesterol less common than lipemia, and reported normal observations in most cases. Bloor,[8] on the other hand, found that all blood lipoids (fat, cholesterol and lecithin) were higher in diabetic lipemia, although fat showed the greatest increase.

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TABLE 1.—*Blood Cholesterol in Diabetic Children*

Case	Age	Blood				Food*				Tolerance†	
		Cholesterol	Fat	Sugar	Ketonuria	Fat, per Cent	F.A. - D. Ratio	Calories, per Pound	Weight§	Units per 10 Gm.	Units
J. H.	8	213.6	1,247	..	0	69	1-1	31	—10	C133	0
	8	208.3	2,185	83	++	69	1-1	31	—10	C133	0
	8½	150	378	74	+	69	1-1	30	+ 3	C143	0
	9	154.3	328	71	0	68	0.8-1	27	+ 4	C178	0
W. D.	12	186	523	87	0	79	1.5-1	30	+ 2	C142	0
	12½	142	608	95	0	74	1.4-1	29	+ 2	C157	0
	12½	142.8	493	90	0	72	1.16-1	28	+ 2	C157	0
	13	217.4	.....	160	+	70	1-1	27	+ 4	C172	0
M. W.	12	137.3	869	...	—	75	1.4-1	23	0	2.5	30
	12¼	170	592	270	—	75	1.4-1	25	0	2.8	32
	12¾	185	603	80	0	75	1.4-1	32	—12	3.4	45
	12¾	172.4	505	200	—	75	1.4-1	28	0	3.4	45
	13	178.5	3,333	464	++++	Coma; dextrose only					
R. M.	10	208	549	180	—	79	1.4-1	22	+ 1	1.9	20
	10¼	238	.....	...	—	79	1.4-1	..	+ 2	4.4	46
	10½	303	1,189	181	+	79	1.4-1	21	+ 4	4.6	48
	11	238	987	111	0	79	1.4-1	19	+ 7	4.4	46
G. A.	12	174	359.8	111	—	79	1.6-1	27	— 1	0.37	5
	12½	192	683	105	0	64	1.2-1	27	— 1	0.41	5
M. N.	12	173	396	100	0	84	1.6-1	..	0	0.9	10
	12¾	171.2	888	83	0	76	1.6-1	21	— 3	0.8	5
	13	176	608	110	0	69	1.2-1	21	— 8	0	0
S. H.	8	170	2,000	138	+	76	1.45-1	31	+ 1	2.8	42
	8½	185	555	91	0	76	1.45-1	29	+ 8	1.8	32
N. A.	12	158.3	660	170	+	75	1.45-1	31	—18	4.9	63
	12¾	169	766	...	+	79	1.4-1	27	—18	4.9	63
	13¼	151.2	1,185	181	++	79	1.4-1	23	— 5	4.1	52
F. Z.	10	185	635	360	0	70	1.3-1	29	+13	?	?
	11½	153	1,180	266	0	General diet			....	?	90†
C. L.	13	163	1,320	133	+	70	1.5-1	25	+ 2	4.5	58
	13	175.6	.....	...	+	70	1.5-1	25	+ 2	4.5	58
Mi. B.	8	250	370	71	0	77	1.3-1	47	—20	124	0
	8½	181	555	60	0	67	0.9-1	48	— 7	154	0
B. P.	14	179	862	190	+	74	1.4-1	21	— 1	4.7	54
	14¼	145	339	190	+	70	1.1-1	17	— 7	4.7	54
	14¾	140.3	1,367	240	+	70	1.1-1	18	— 7	2.6	25
E. L.	10	191	1,212	444	++++	Coma			—34		
	10	200	370	112	0	73	1.3-1	39	—28	3.2	41
M. We.	11	227	3,418	450	++++	Coma					
	11¼	192.8	592.5	68	0	72	1.45-1	31	— 4	1.7	24
A. G.	13	148	.....	116	0	..	1.55-1	24	+ 8	1.2	10
	13½	256	480	...	0	73	1.55-1	21	+15	1.3	18
	13¾	217	716	133	0	73	1.5-1	21	+18	1.5	20
	13¾	156	962	173	—	73	1.5-1	21	+18	1.5	20
	14	153	1,048	205	+	74	1.3-1	28	+10	2.6	23
M. M.	9	193	800	63	0	76	1.48-1	37	— 6	C117	0
	9½	238	494	91	0	76	1.48-1	31	0	C117	0
	9¾	221	1,111	87	0	76	1.48-1	30	+ 3	C117	0
	9¾	200	1,333	86	0	76	1.48-1	30	+ 3	C117	0
	10¼	205	522	69	0	71	1.15-1	30	0	C148	0
W. D.	8	117	1,320	82	0	74	1.4-1	35	—20	...	5
	8	250.6	1,490	111	0	74	1.4-1	35	—20	0.4	5
	8¼	277	630	210	+	74	1.4-1	30	— 6	0.04	1
	9	357	639	60	0	74	1.4-1	31	— 7	1.0	12
P. B.	7	164	666	202	+	70	1.4-1	..	....	1.8	18
J. P.	8½	133	419	129	0	60	1.3-1	45	—20	C128	0
W. Da.	7	196.7	.....	100	0	72	1.28-1	37	—10	C105	0
D.D.	4	135	383	90	0	70	1.3-1	33	0	C110	0
B. L.	10	199	740	225	++	66	1.4-1	25	+ 3	3.5	50
R. C.	3	166	574	75	0	64	1-1	42	8	C120	0

* Percentage of fat in the food equals percentage of total energy intake derived from fat.

Ratio of fatty acids to dextrose (F.A. - D.) = $\frac{\text{90\% fat + 40\% protein}}{\text{100\% of dextrose + 58\% of protein + 10\% of fat}}$

§ Variations of weight represent the deviation of the normal for height and age.

† Under tolerance, C followed by a figure equals the number of grams of total carbohydrate the patient could tolerate.

TABLE 1.—*Blood Cholesterol in Diabetic Children—Continued*

Case	Age	Blood			Keto-nuria	Food*				Tolerance†	
		Choles-terol	Fat	Sugar		Fat, per Cent	F.A. - D. Ratio	Calories, per Pound	Weight§	Units per 10 Gm.	Units
F. S.	2	277	888	367	++++	Dextrose only					
W. W.	3	171	421	95	+	67	1-1	33	+11	2.1	27
T. B.	7	187	1,111	59	0	74	1.26-1	36	— 1	0.64	7
G. M.	3	247.6	1,646	330	+++	75	1.2-1	39	+ 1	3.7	34
D. S.	7	187.5	.....	85	0	64	1.3-1	40	0	C120	
E. D.	10	260	808	181	—	67	1.2-1	32	0	2.2	29
A. M.	12	161	434	454	+++	73	1.2-1	31	—12	2.7	39
M. Bu.	11	176	345	56	0	86	1.4-1	26	— 9	1.8	26
J. Da.	13	157	959	121	0	75	1.5-1	24	— 1	C125	
M. Bo.	10	178.5	2,222	190	++++	70	1.2-1	29	+ 4	2	25
B. G.	12	227	1,220	343	++++	70	1.3-1	26	0	1.4	18
M. Wa.	3	200	1,975	445	++++	64	0.9-1	67	—30	1.7	20
A. R.	6	229	1,185	91	0	65	1-1	33	0	C108	
G. W.	11	277	808	64	+	74	1.2-1	32	— 7	2.0	64
	11	263	.....	66	0	74	1.2-1	32	— 6	2.0	64
Ja. W.	9	250	757								

* Percentage of fat in the food equals percentage of total energy intake derived from fat.

Ratio of fatty acids to dextrose (F.A. - D.) = $\frac{90\% \text{ fat} + 40\% \text{ protein}}{100\% \text{ of dextrose} + 58\% \text{ of protein} + 10\% \text{ of fat}}$

§ Variations of weight represent the deviation of the normal for height and age.

† Under tolerance, C followed by a figure equals the number of grams of total carbohydrate the patient could tolerate.

TABLE 2.—*Cholesterol in Patients with Lipemia and in Those with Normal Blood Fat*

Plasma Cholesterol Mg. per 100 Cc.	Blood Fat, Mg. per 100 Cc. of Plasma		
	Normal	700-1,000	1,000 or Over
Maximum	250	222	303
Minimum	111	119	111
Average	153	186.9	182.8

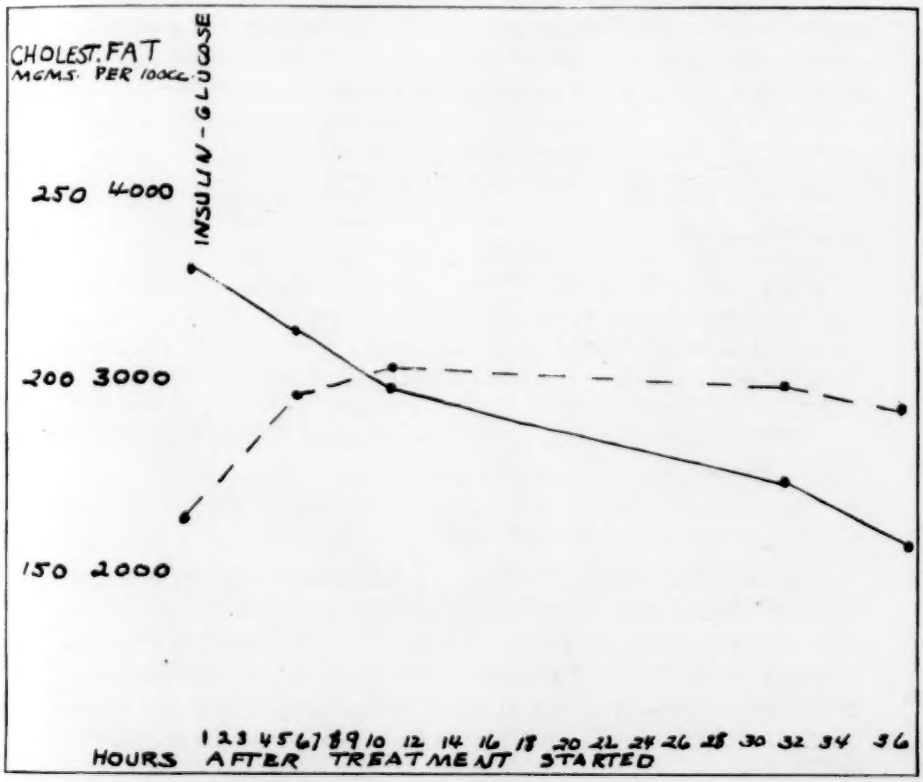
This held true whether the lipemia was derived from endogenous or exogenous fat. The hypercholesteremia in ten cases persisted after the lipemia had disappeared.

The plasma cholesterol was studied in about ninety diabetic children at the Hospital for Sick Children. In many no deviation from the normal was ever noted. The figures obtained varied from a minimum of 110 to 375 mg. per hundred cubic centimeters of plasma. Hypercholesteremia was found sufficiently often that the average figure obtained in diabetic subjects was raised. Its presence was much less common than lipemia in the children studied.

Lipemia is not always associated with hypercholesteremia. This may be due, in part, to the observations which Bloor has made that the fat increases first. Certain cases in which I was able to study the development of the lipemia, such as that shown in the accompanying chart, show that the rise in cholesterol not only occurs later but disappears more

slowly. The figures given in table 2, however, indicate that in general, the blood cholesterol is only slightly greater in patients with lipemia than in those with normal blood fat.

The plasma cholesterol in the same subject does not vary directly with the blood fat, nor does it always increase in lipemia, unless the latter is severe or persistent. When the cholesterol does increase in lipemia, the increment occurs more slowly and is relatively smaller, and the return to normal is more gradual than in the case of fat.



Rise in cholesterol with development of lipemia.

No relationship between the presence or absence of turbidity of the serums and the cholesterol content is demonstrable.

BLOOD CHOLESTEROL IN ACIDOSIS

The plasma cholesterol was studied in six cases of diabetic coma. In two of these it was at a low normal level when the child was admitted to the hospital, and although it increased slightly before the lipemia disappeared, it did not at any time exceed the normal level. The average

figure obtained in these cases was a little over 200 mg. per hundred cubic centimeters, and the maximum was 357 mg. per hundred cubic centimeters. Usually the plasma fat was at its maximum at the time of admission, whereas the cholesterol continued to rise until after the fat content began to decrease.

In patients with chemical evidence of acidosis but not necessarily presenting clinical symptoms of such, the plasma cholesterol is usually increased somewhat. This is shown in the figures in table 3, in which the degree of acidosis is indicated by the degree of ketosis present. In patients with a severe degree of acidosis, in whom it was possible to obtain a positive Rothera test on the blood plasma, the cholesterol content of the blood averaged 215 mg. per hundred cubic centimeters.

TABLE 3.—*Cholesterol in Patients with Acidosis*

	Acetonuria (Rothera Test)	
Plasma Cholesterol	0–++	+++ or More
Maximum	262	357
Minimum	111	162
Average	175	224

TABLE 4.—*Cholesterol in Normal and Undernourished Children*

Weight	Average Plasma Cholesterol
Normal	185
10 per cent above normal	193
10 per cent below normal	194
20 per cent below normal	202

The relative increase in the blood cholesterol in acidosis is not of the same magnitude as that of the blood fat, and as pointed out before, both its rise and fall are slower. Patients who persistently had ketosis showed a tendency toward the slow development of hypercholesteremia. The number of the latter type of cases studied was not large. A similar rise in plasma cholesterol occurs in patients with persistent lipemia.

BLOOD CHOLESTEROL AND BODY WEIGHT

In view of the fact that the only abnormalities found by Denis in the blood cholesterol of diabetic patients appeared to be dependent on variations in weight, I studied the effect of deviation from normal weight of 10 per cent or more. Wide variations in the blood cholesterol occurred in each weight group. As will be seen from the figures in table 4, the average value for cholesterol in extremely malnourished children is somewhat higher, but the increases hardly appear great enough to be significant. The deviations from normal weight are based on a consideration of the latter from the standpoint of both the height and the age.

BLOOD CHOLESTEROL AND FOOD

The effect of food on the plasma cholesterol is of interest because of the unsettled question of the part cholesterol plays in fat metabolism. It has been demonstrated by Shope [9] and others that the fasting cholesterol is relatively high and may be reduced by feeding a mixed meal. This author [10] has more recently demonstrated by animal experiment that this reduction follows the separate administration of fat, carbohydrate or protein as well as a mixed meal. Further a diet of fat alone for forty-eight hours causes no significant rise in the plasma cholesterol. Beumer [11] found a wide independence of hypercholesteremia and diet, in that a diet poor in lipoids did not decrease nor did one rich in lipoids increase the plasma cholesterol in the postabsorptive period. György [12] was unable to induce alimentary hypercholesteremia.

In my cases, high fat diets did not cause hypercholesteremia, nor did lowering the fat intake reduce a previously high plasma cholesterol. The diets used derived from 64 to 84 per cent of their energy value from fat. Their ketogenic antiketogenic ratio varied from 0.8:1 to 1.6:1. It was pointed out in a previous paper [13] that excessive caloric intake exerted more effect on the production of lipemia than did the fat content of the diet. Such a relationship between plasma cholesterol and energy intake was not demonstrable.

BLOOD CHOLESTEROL AND BLOOD SUGAR

McCrudden and Sargent [14] studied the relationship between blood sugar and blood cholesterol in thirty-six cases and concluded that no consistent relationship existed. My observations would corroborate these results in the main. In any patient variations in blood sugar from normal to over 300 mg. per hundred cubic centimeter of plasma were unaccompanied by similar rises in cholesterol.

The comparison of blood sugar value and cholesterol value during fasting does show some tendency toward a consistent relationship between the two. Rabinowitch [15] pointed out that in patients with high values for blood sugar during fasting independent of their insulin requirement, the blood cholesterol is also high. As the figures in table 5 show, this held true in my cases when average values were taken. Wide individual variations, however, occurred.

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BLOOD CHOLESTEROL AND BLOOD PROTEIN

There appears to be a more consistent relationship between blood protein (refractometer) and blood cholesterol than between the latter and any other variable studied. The cholesterol was nearly always high when the blood protein was low (less than 7 per cent). The average cholesterol with high or normal protein was 187 mg. per hundred cubic centimeters, whereas in cases with a low protein content, the average was 209 mg. per hundred cubic centimeters. The significance of this relationship has not been determined.

TABLE 5.—*Cholesterol in Relation to Values for Blood Sugar During Fasting*

Plasma Cholesterol	During Fasting		
	Normal Blood Sugar	Blood Sugar Less Than 180	Blood Sugar More Than 180
Maximum	229	260	303
Minimum	110	170	111
Average	165	193	201

TABLE 6.—*The Initial Blood Cholesterol in Diabetic Children*

Case	Age	Cholesterol in Gm. per 100 Cc.	Comment
M. B.	5	250	Mild case needing no insulin; complicated by mediastinal tuberculosis
J. D.	12	156.7	Mild case; progress favorable with diet alone
M. B.	8	178.5	Moderately severe case at first; always required insulin; much worse because of failure to cooperate
B. G.	12	227.2	Moderately severe, requires insulin; complicated by mediastinal tuberculosis
M. W.	9	162	Moderately severe at first; has retrogressed because of infidelity to diet
M. We.	10	227	Severe case
W. D.	9	147	Moderately severe; requires small doses of insulin
S. M.	6	183.1	Severe case
R. C.	2	166	Mild case; easily treated by diet alone
B. P.	14	179	Severe case
G. M.	2	247.6	Moderately severe case; does well and tolerance improved on diet plus insulin
E. L.	9	111	Severe case; was 35 per cent underweight at time of this test
E. D.	9	260	Moderately severe; progress favorable on diet plus insulin
G. W.	11	277	Severe case
J. W.	9	250	Severe case

BLOOD CHOLESTEROL AND PROGNOSIS

The initial blood cholesterol was determined in twenty-two cases of diabetes, 72 per cent of which required insulin. Nine of eleven patients with an initial figure in excess of 200 mg. per hundred cubic centimeters had severe diabetes, one had mediastinal tuberculosis and the other had a severe degree of undernutrition and lipemia; however, both the hypercholesteremia and the lipemia disappeared at a later date when the nutrition improved. Severity of the disease, however, was not always associated with hypercholesteremia, as in many severe cases the patients had normal cholesterol values and approached the abnormal only during periods of acidosis and lipemia. Thus while my figures would bear

out the contention of Rémond [16] and others as to the serious import of hypercholesteremia, its absence does not warrant classifying the case as mild. Initial cholesterol values appear to vary more with the degree of acidosis present than with the inherent severity of the disease process.

Severity when judged by insulin requirement further evidences a tendency for severe diabetes to be associated with hypercholesteremia. Seventy-one per cent of patients needing no insulin have normal blood cholesterol, whereas only 50 per cent of those needing insulin are normal. As shown in table 6, however, the height of the cholesterol and the amount of insulin required bear no direct relationship to one another.

The relationship between plasma cholesterol and the advance or retrogression of the diabetes has been studied by several observers.[17] Rabinowitch assumed from his studies that hypercholesteremia is incompatible with improvement in tolerance. This incompatibility of high cholesterol and increasing tolerance was more demonstrable in the patients treated with insulin than in those in whom the condition was mild enough to require no insulin. In spite of steady gains in tolerance, five of the latter patients had a persistent mild hypercholesteremia during the first one and a half or two years of treatment. It would almost appear that in such cases fat combustion even in the absence of hyperglycemia was less perfect than in cases in which the patients were treated with insulin, and that the higher fat diets used during this period were at least a factor in producing a rise in blood cholesterol. Subsequently, when improved tolerance permitted the use of more carbohydrate and less fat, the blood cholesterol gradually became normal.

I was unable to confirm the observation made by Rabinowitch, that in patients with a high amount of blood cholesterol the slightest illness or dietary excess resulted in a more persistent hyperglycemia than in those with a normal amount of cholesterol.

SUMMARY

1. Hypercholesteremia is present in only a small proportion of diabetic children.

2. Hypercholesteremia and lipemia are not necessarily associated in the same case. When the lipemia is chronic, the plasma cholesterol tends to rise.

3. The increase and decrease of blood cholesterol in severe lipemia are slower than the rise and fall of the blood fat.

4. The blood cholesterol remains nearly constant in the same subject.

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5. Patients with clinically severe acidosis or a severe grade of ketonuria usually have an increased blood cholesterol, but the magnitude of this increase is usually less than that of the blood fat.

6. The height of the plasma cholesterol and its degree of turbidity showed no relationship to one another.

7. There is a tendency toward hypercholesteremia in severe grades of malnutrition.

8. The plasma cholesterol bears no relationship to the amount of fat ingested.

9. The plasma cholesterol and the blood sugar bear no constant relationship to one another, but high fasting blood sugars are associated with higher maximum and average cholesterol values.

10. High blood cholesterol is usually found in cases of hydremia.

11. Hypercholesteremia usually indicates diabetes sufficiently severe to require insulin in the treatment, but low plasma cholesterol does not necessarily indicate that the case is mild.

12. The height of the blood cholesterol is not directly proportional to the amount of insulin required.

13. Hypercholesteremia is not incompatible with improving tolerance but is more often seen in patients not treated with insulin who are progressing favorably than in those treated with insulin who are pursuing a similar course.

GROWTH OF INFANTS FROM THE STANDPOINT OF PHYSICAL MEASUREMENTS AND OF NITROGEN METABOLISM

II. CREATINE *

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AND
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Urinary creatine, which in the adult is found only in exceptional cases, for example in inanition, occasionally in women and in certain types of disease in which the catabolic processes are accelerated, is a constant and seemingly normal associate of creatinine in the urine of children up to the age of puberty. Of the various theories advanced in explanation of this, the most generally accepted is that the immature muscle, although producing no more creatine per unit of muscle mass than the adult, has a lower capacity for retaining it. Other theories, with the experimental evidence supporting them, have been thoroughly reviewed by Hunter.[1]

The variation in the amount of creatine excreted in normal children appears to be influenced by a number of factors, for example, the amounts of creatine and of protein ingested, and the periodicity of the food intake which may result in shorter or longer periods of depletion of carbohydrate.

According to Mendel and Rose, and Rose,[2] "carbohydrate hunger" may produce a condition resulting in improper functioning of the tissue cells and an inability completely to catabolize the creatine formed. In young children, the metabolic rate is high, the food is quickly digested and absorbed and hunger periods may be frequent, although of short duration. On the other hand, very young children, especially infants who are receiving the usual type of artificial feeding mixtures, are getting diets containing relatively large amounts of protein, which,

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* From the Department of Nutrition, Child Welfare Research Station, State University of Iowa.

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according to Folin and Denis,[3] Denis and Kramer,[4] Harding and Gaebler [5] and others, are responsible for the creatinuria of children. The diurnal variations and irregular outputs have been explained on the basis of the ingestion of food [6] and, in the case of infants, the flushing out process resulting from the large intake of water.[7]

In young children, also, the creatine of cow's milk may have some influence on the output of urinary creatine, since they are having their food requirements met largely from milk.[8] Gamble and Goldschmidt,[8] investigating the relation of the intake of protein to the excretion of creatine in infants, observed that the urinary output of creatine seemed to be related to the quantity of whey ingested. In accord with these observations are those of Denis and Minot,[9] who reported from 2 to 2.6 mg. of creatine in 100 cc. of milk.

In a series of studies of the nitrogen metabolism of infants, it was deemed of interest to consider the output of creatine in relation to those factors which have been suggested as influencing its excretion.

MATERIAL AND METHOD

The eleven infants studied were between 2 and 8 months of age. The number of metabolic studies of each infant ranged from two to ten. For each infant, in each study, daily determinations of the amounts of creatine and creatinine, as well as of the total nitrogens, were made on the twenty-four hour collections of urine of each day for a three day period. The averages of the determinations of the three days are reported.

During the first part of the investigation, the determinations of the creatine were made according to the method of Benedict and Myers,[10] and later according to Folin's modification.[11] The two methods checked closely, but since the autoclaving involved in the former process resulted in a slight amount of caramalization, the method of Folin was preferred. The creatinine values were determined according to the micromethods of Folin,[11] and the total nitrogen values by the Kjeldahl method.

The infants in all cases received artificial feedings, consisting of modifications of cow's milk. In general, dextrimaltose was used as the carbohydrate modifier. In a few cases, lactose or Mellin's food was substituted for a part of the dextrimaltose. The feeding mixtures were either boiled or pasteurized by the closed method. A number of different substances, for example, wheat germ extract, yeast extract tablets and lactic acid, were used in the feeding mixtures in order to determine their influence on the retention of nitrogen. These do not appear

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to have influenced the eliminations of creatine. The effect of irradiated milk, as well as of dried milk, also was tested. The results with S.M.A., a modification of cow's milk in which the protein is low and in which the fat has been made to resemble more nearly that of human milk, illustrate the influence on creatine excretion of a feeding mixture containing little protein. Besides the milk feedings, the infants received, daily, orange juice and cod liver oil, with the exception of a few in whose case the latter was discontinued shortly before and during the period of study of metabolism. The feeding schedules (every three hours during the day and every four hours at night) were the same in all but two cases, thus ruling out the variations resulting from possible carbohydrate depletion.

In the tables, which give the results of the investigations, we have included, besides the average amounts of creatine, creatinine and nitrogen eliminated, the amounts of nitrogen ingested, as a general measure of the amounts of possibly exogenous creatine. In a number of cases (table 2) the daily volumes of urine have been given in order to show to what extent these may have influenced the elimination of creatine.

RESULTS AND COMMENTARY

The amounts of creatine eliminated by the infants varied greatly. There was no apparent relation between the amounts of creatine and of creatinine eliminated, nor between the amount of creatine excreted and age. The lowest amount of creatine eliminated was 24 mg., by baby B. C. at 4 months and 7 days, with an excretion of creatinine of 78 mg. The highest amount was 153 mg., by baby J. M. at 6 months and 2 days, with an elimination of creatinine of 86 mg. The youngest infant, baby J. M., with a urinary output of creatinine of 63 mg. at 1 month and 28 days, excreted 82 mg. of creatine; whereas the oldest infant, baby P. H., with a urinary output of creatinine of 112 mg. at 7 months and 21 days, excreted 85 mg. of creatine.

Our observations relative to the elimination of creatine are not in accord with those of Rougichitch,[7] who reported that the total excretion of creatine in twenty-four hours approaches the total excretion of creatinine. In only one case in our series, that of baby E. M., was there any parallelism, and this seems to have been due to the fact that the same type of feeding was given throughout the seven periods of study of its metabolism, the only variation being the increase in the amount of milk ingested as the infant grew older. The increase in the elimination of creatine and the close parallelism between this and the excretion of creatinine may be related to the increase in the ingestion of protein and the normal increase in the elimination of creatinine which is coexistent with the development of muscle. There is not necessarily any inherent relation between the production of creatine and that of creatinine. With one exception, the elimination of creatine by baby P. H. at a given level of ingestion of protein remained fairly constant, in spite of the fact that the output of creatinine increased as the infant grew older.

TABLE 1.—*The Relation of Ingestion of Nitrogen to Excretion of Creatine, Creatinine and Nitrogen in Infants*

Infant	Age		Weight, Kg.	Creatinine Preformed, Mg.	Creatine as Creatinine, Mg.	Nitrogen in Urine, Gm.	Nitrogen Intake, Gm.	Feeding *
	Months	Days						
B. W.	3	7	6.36	67	61	2.19	3.38	Pasteurized
	3	18	6.55	74	51	2.66	3.38	Pasteurized
	3	26	6.89	75	64	2.58	3.06	Boiled
N. W.	3	15	6.83	73	68	2.62	3.33	Pasteurized
	3	25	7.11	76	75	2.53	3.33	Pasteurized
	4	3	7.60	82	67	2.79	3.53	Boiled
	4	17	8.10	87	89	2.24	3.53	Boiled; extract of wheat germ
	5	29	9.29	96	111	3.66	4.63	Boiled; Mellin's food
J. A.	3	20	5.56	63	78	2.26	3.33	Pasteurized
	4	0	5.93	66	87	2.55	3.33	Pasteurized
	4	8	6.23	67	74	2.36	3.53	Boiled
	4	21	6.66	71	95	2.36	3.53	Boiled; extract of wheat germ
	6	0	7.29	73	119	3.14	4.17	Boiled; Mellin's food
L. T.	3	21	5.53	58	65	2.61	3.33	Pasteurized
	4	0	5.85	64	63	2.56	3.33	Pasteurized
	4	14	6.01	69	68	2.73	3.35	Boiled
	4	23	6.33	80	57	2.96	3.53	Boiled
	5	11	7.00	62	84	2.49	3.53	Boiled; extract of wheat germ
	6	0	7.14	71	100	2.91	4.05	Boiled; Mellin's food
B. C.	4	7	5.50	78	24	2.17	3.32	Boiled; extract of wheat germ
	4	14	5.66	77	43	2.11	3.32	Boiled
	5	6	6.36	83	33	2.39	3.53	Boiled; extract of wheat germ
	5	23	6.84	81	33	2.41	3.53	Boiled; irradiated; extract of wheat germ
R. C.	2	6	4.84	57	54	1.94	2.87	Boiled
	2	15	5.09	53	43	1.76	2.39	Boiled; extract of wheat germ
	3	4	5.55	55	71	2.62	3.64	Boiled; Mellin's food
	5	12	6.85	72	54	2.48	3.69	Boiled; lactose; extract of wheat germ
	5	19	6.96	79	52	2.43	3.69	Boiled; lactose
	6	29	7.56	80	48	2.41	4.11	Boiled; irradiated; extract of wheat germ
M. E.	2	26	5.58	65	38	1.78	2.88	Boiled; irradiated
	3	21	6.00	71	38	1.08	1.98	S. M. A.
	4	16	6.50	74	43	2.21	3.01	Pasteurized
	4	24	6.75	77	38	2.48	3.01	Pasteurized
	5	0	6.83	81	40	2.40	3.32	Boiled
	5	16	7.05	85	25	2.16	2.91	Boiled; "B" tablets
	5	29	7.03	91	47	2.09	3.01	Boiled; irradiated; "B" tablets
A. R.	4	25	7.50	93	39	2.75	3.75	Boiled; lactic acid
	5	11	7.75	97	41	2.98	3.62	Boiled
P. H.	2	13	6.08	73	66 †	2.31	3.67	Boiled
	2	21	6.50	79	70	2.81	3.67	Boiled; lactic acid
	3	0	6.80	79	80	2.63	3.76	Boiled; lactic acid
	3	26	7.37	82	70	2.67	3.76	Boiled
	5	0	8.50	108	85	3.80	4.93	Dried
	5	8	8.82	112	76	3.75	4.93	Dried; extract of wheat germ
	6	0	9.30	117	85	4.00	4.93	Dried; irradiated
	7	0	9.60	111	107	4.10	4.93	Dried; irradiated
	7	8	9.80	123	86	4.19	4.93	Dried
	7	21	9.95	112	85	3.68	4.54	Boiled
J. M.	1	28	5.40	62	82	2.07	2.68	Boiled
	3	1	6.00	67	81	1.37	2.21	S. M. A.
	3	10	6.35	69	133	2.37	3.55	Boiled; extract of wheat germ
	4	7	7.00	76	128	2.54	3.78	Boiled; irradiated
	4	22	7.48	77	142	2.86	3.86	Boiled; "B" tablets
	5	6	7.60	77	119	2.71	3.85	Boiled; extract of wheat germ
	5	21	7.85	78	83	1.54	2.21	S. M. A.
	6	2	8.15	86	153	3.58	4.98	Boiled; Mellin's food
	6	17	8.45	95	128	3.53	4.52	Dried
E. M.	2	14	5.65	66	61	1.90	3.42	Boiled
	2	25	6.05	70	78	2.29	3.40	Boiled
	3	10	6.50	72	87	2.42	3.40	Boiled
	3	25	7.00	84	88	2.50	3.64	Boiled
	4	7	7.15	86	94	2.39	3.64	Boiled
	4	14	7.45	91	107	3.05	4.09	Boiled

* The method of treating the milk and the additions used are indicated.

† The previous determinations of creatine were made by the method of Benedict and Myers; the following, by the method of Folin.

The theory of Rose [2] that "carbohydrate hunger" is a causative factor in the creatinuria of infancy seems to be untenable in view of our observations. The feeding mixtures used were calorically adequate, as indicated by the gains in weight during the periods of study of metabolism, and since all infants were fed at the same frequent intervals, the variations cannot be attributed to periods of depletion of carbohydrate.

TABLE 2.—*The Relation of the Daily Excretion of Creatine to the Intake of Liquids and Volume of Urine in Infants*

Infant	Age		Urine, Cc.	Creatinine Preformed, Mg.	Creatine as Creatinine, Mg.	Milk, Cc.*
	Months	Days				
E. M.	2	8	450	66	61	650 †
	2	14	445	67	61	650
	2	15	440	65	60	650
	2	25	495	70	84	650
	2	26	430	69	67	650
	2	27	485	84	83	650
	3	10	475	74	75	700
	3	11	455	71	99	700
	3	25	525	86	130	700
	3	26	550	84	84	700
	4	8	350	87	83	700
	4	9	415	87	101	700
	4	15	430	95	108	800
P. H.	3	27	540	81	65	700 †
	3	28	565	81	53	700 †
	5	0	444	105	92	120 Gm. dried
	5	1	445	108	86	120 Gm. dried
	5	2	428	110	77	120 Gm. dried
	5	8	265	113	80	120 Gm. dried
	5	10	360	110	88	120 Gm. dried
	5	29	375	118	79	780 Gm. dried ‡
	5	30	380	116	85	120 Gm. dried ‡
	6	0	475	116	92	120 Gm. dried ‡
	7	21	420	113	131	850 ‡
J. M.	3	2	480	68	86	440 cc. S. M. A.
	3	11	480	69	137	650
	4	8	580	75	131	700
	4	9	555	68	95	700
	4	22	538	75	147	700
	4	24	540	79	147	700
	5	6	430	80	124	700
	5	8	435	77	128	700
	5	21	300	77	68	430 cc. S. M. A.
	5	22	310	78	94	430 cc. S. M. A. ‡
	5	23	420	78	88	430 cc. S. M. A. ‡
	6	3	440	94	144	800
	6	17	190	99	145	110 Gm. dried ‡
	6	18	325	90	112	110 Gm. dried ‡

* Unless otherwise designated, the milk was diluted with water and distributed among seven feedings of 150 cc. each.

† Seven feedings of 140 cc. each.

‡ Six feedings of 150 cc. each.

Nor can these variations in the output of creatine be due to the flushing out of the catabolic creatine. The amount of liquid taken varied slightly with the different infants, but this seemed to have no relation to the amount of creatine eliminated. The volume of urine also seemed to bear no relation to the output of creatine. A low volume sometimes carried a high content of creatine, or a high output of urine little creatine. This lack of correlation between volume of urine and output of creatine is especially noticeable in the case of baby J. M.,

who at 6 months and 3 days put out 440 cc. of urine with a creatine content of 144 mg.; two weeks later, he excreted practically the same amount of creatine in 190 cc. of urine.

Apparently, the creatine content of milk also is not an important factor in influencing the output of creatine in infancy. The largest quantity of milk ingested in any twenty-four hour period was 850 cc., by baby P. H. at 7 months and 21 days, which, according to Denis and Minot's estimate,[9] carries from 17 to 22 mg. of creatine, an amount much too low to account for the creatine values observed. And although the excretion of creatine increased with the larger ingestions of milk, there was no definite relation between the amount of milk ingested and the amount of creatine eliminated by the various infants. For example, baby B. C., with an intake of milk of 700 cc. eliminated 33 mg. of creatine during two successive periods of study, whereas baby J. A., at 4 months and 8 days, receiving the same amount of milk, excreted 74 mg. of creatine, and baby L. T., at 4 months and 23 days, who also was receiving 700 cc. of milk, excreted 57 mg. of creatine. Obviously, the ingestions of milk cannot explain the variations in these excretions of creatine.

The influence of the amount of protein ingested on the amount of creatine eliminated, observed by a number of investigators, seems to be borne out by the results with the infants receiving the simple milk mixtures. The parallelism between the urinary output of nitrogen, as a measure of the absorption of protein, and the urinary output of creatine is quite consistent for a given child. With the infants receiving the Mellin's food mixture, the influence of the amount of protein ingested was particularly noticeable. In every case, an increase in the protein in the food was followed by an increase in the nitrogen and creatine in the urine. On the other hand, the infants receiving the S.M.A. feedings, which supplied considerably less protein than these infants received during previous and subsequent periods, showed, in one case (baby J. M. at 5 months and 21 days), a distinctly lower output of creatine. With two infants (baby M. E. and baby J. M.), the outputs of creatine were comparable with those of the preceding periods, approximately one month before, but considerably lower than those during the two successive periods, which, in one case, was ten days later and in the other nearly one month later. An ingestion of smaller amounts of protein on a simple boiled feeding (baby M. E. at 5 months and 16 days) also resulted in an output of smaller amounts of creatine.

Although the ingestion of protein appears to influence the elimination of creatine, there seems to be no definite relation between the amount of protein ingested and the amount of creatine excreted. This relationship differs with different infants, but is fairly constant for a given infant. For example, baby J. M. excreted much more creatine

than baby P. H., even though he was receiving somewhat less protein. The amount of creatinine eliminated by baby J. M. at the same age level was considerably less than that eliminated by baby P. H. If we can accept creatinine as a measure of muscle mass, it would seem from these results that there is a fairly close relationship between the amount of muscle tissue and the amount of creatine or creatine precursors that can be either produced or retained at a given level of ingestion of protein. Viewing our data from this standpoint, however, we find little to support the hypothesis. Baby B. C., at 5 months and 6 days of age, with a creatinine output of 83 mg., excreted 33 mg. of creatine, whereas baby E. M., at 3 months and 25 days, with approximately the same urinary output of creatinine and a slightly higher output of nitrogen, excreted 88 mg. of creatine. These variations seem to be beyond the limits of error of the method used. Similar wide variations can be found among the other infants. If muscle metabolism were concerned wholly with creatine metabolism, one would expect to find the muscle mass in a given child, as determined by the output of creatinine, capable of producing or storing a definite amount of creatine; therefore, two different children eliminating the same amounts of creatinine at a given level of protein should excrete approximately the same amounts of creatine. We do not find such to be the case. Our results seem to indicate that although the urinary creatine is related to protein metabolism, the creatine is largely of exogenous origin, possibly an intermediary product of amino-acid catabolism, a certain amount of which is essential to physiologic processes. In infants receiving diets rich in protein (largely casein), more is formed than is needed. This is excreted. These views are in accord with those of McCollum and Steenbock[12] and Steenbock and Gross:[13] "Creatine is an end-product in the catabolism of certain precursors in the protein molecule just as urea is of others." If these are "present in excess relative to the demands for protein synthesis," they will be transformed into creatine.[1]

Creatinine, on the other hand, is a waste product of muscle metabolism. The amount excreted increases gradually with increasing age. The excretion of creatinine is unrelated to the ingestion of protein. The two substances, creatine and creatinine, appear to be related only as one (creatine) is a normal nitrogenous catabolic substance, a certain amount of which is essential, possibly, to cell metabolism, whereas the other (creatinine) is a nitrogenous end-product of muscle metabolism.

The creatinuria of infants receiving artificial feeding mixtures appears to be directly related to the relatively high amount of protein in the feeding mixtures.

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12. McCollum, E. V., and Steenbock, H.: J. Biol. Chem. **13**:209, 1912.
13. Steenbock, H., and Gross, E. G.: J. Biol. Chem. **36**:265, 1918.

SUMMARY

In a series of studies of the metabolism of eleven normal infants receiving artificial feedings of modifications of cow's milk, it was observed that the amount of creatine excreted bore no relation to age, development of muscle, as indicated by the amounts of creatinine eliminated, or to volume of urine. The intake of food was so controlled that the factor of possible depletion of carbohydrate was excluded.

The results of the investigation seem to indicate that the creatinuria of infancy is related to the ingestion of protein. An increase in the urinary nitrogen, in general, was coexistent with an increase in the urinary creatine. It is suggested that creatine is an end-product in the catabolism of certain precursors in the protein molecule, and bears no relation to the urinary creatinine, which is an end-product of muscle metabolism.

GROWTH IN INFANTS FROM THE STANDPOINT OF PHYSICAL MEASUREMENTS AND NITROGEN METABOLISM

III. URIC ACID *

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In infants, endogenous uric acid has been shown to be excreted in much larger amounts proportionately than in adults. This appears to be due, in part, at least, to the relatively larger amount of glandular tissue, which comprises nearly one half of the total body substance of the infant. Other factors, for example, the amount of protein ingested and possibly the amount of carbohydrate, which in the adult has been shown to stimulate cellular metabolism, may have some influence. Roughichitch suggested that in the artificially fed infant the excretion of high amounts of uric acid may be the result of the proportionately high intake of protein, although in his recent study he did not find a close relationship between the urinary nitrogen and uric acid.[2] Orgler [3] believed that the lower output of uric acid of the breast-fed infant is due to the better utilization of the ingested food. Utheim [4] and Rougichitch,[5] however, found no relation between abnormal nutritional conditions and elimination of uric acid, except in the case of an infant suffering from rickets (Rougichitch) whose output of uric acid was considerably higher than that of the other infants studied.

In an investigation of the metabolism of artificially fed infants, we have examined the excretion of uric acid in three artificially fed infants in order to determine its relation (1) to growth, (2) to the food ingested and (3) to other nitrogenous constituents of the urine.

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* From the Department of Nutrition, Iowa Child Welfare Research Station, State University of Iowa.

* This study was made possible through the courtesy of the Department of Pediatrics, College of Medicine, State University of Iowa.

1. Reference deleted by the author.

2. Rougichitch, O. S.: Uric Acid and Creatinine in the Urine of Infants, Am. J. Dis. Child. **31**: 504 (April) 1926.

3. Orgler, A.: Jahrb. f. Kinder. **57**: 383, 1908.

4. Utheim, K.: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances (Athrepsia), Am. J. Dis. Child. **22**: 329 (Oct.) 1921.

5. Rougichitch, O. S.: Uric Acid in the Urine of Infants: II. Day and Night Excretion, Am. J. Dis. Child. **32**: 530 (Oct.) 1926.

The conditions of the investigation were the same as those in the previous studies of the excretion of creatinine and creatine of normal infants. For the determinations of the values of the uric acid the direct colorimetric method of Benedict and Franke [6] was used.

RESULTS AND COMMENT

In the three infants studied there was found to be a gradual increase in the amount of uric acid excreted as the infants grew older (table 1). The smallest amount, 42 mg., was excreted by the youngest infant,

TABLE 1.—*Excretion of Uric Acid as Related to Weight, Height, Elimination of Creatinine and Intake of Nitrogen*

Infant	Age		Weight,	Height,	Intake of Nitrogen per Day,	Urinary Nitrogen,	Creatinine,	Uric Acid,	Uric Acid Excreted per Kg.,	Uric Acid Excreted per Cm.,
	Mos.	Days	Kg.	Cm.	Gm.	Gm.	Mg.	Mg.	Mg.	Mg.
E. M.	2	8	5.45	57.6	....	....	66	71	13.1	1.14
	2	14	5.65	58.0	2.29	1.90	67	70	12.4	1.20
	2	25	6.05	59.8	3.06	2.29	70	77	12.7	1.46
	3	10	6.50	60.9	3.06	2.42	72	78	11.9	1.28
	3	25	7.00	62.5	3.30	2.50	84	82	11.7	1.31
	4	7	7.15	63.9	3.30	2.40	86	83	11.5	1.30
	4	14	7.45	64.5	4.09	3.05	91	83	11.1	1.72
								Av.	12.0	
J. M.	1	28	5.40	58.4	3.02	2.07	63	42	7.8	0.77
	3	1	6.00	61.4	2.21	1.37	66	48	7.9	0.78
	3	10	6.35	61.9	3.55	2.38	69	52	8.1	0.84
	4	7	7.00	64.6	3.78	2.54	76	80	10.0	1.17
	4	22	7.48	65.1	3.86	2.86	77	79	10.5	1.16
	5	6	7.60	65.8	3.85	2.78	77	90	11.9	1.36
	5	21	7.85	66.9	2.21	1.54	78	114	14.6	1.70
	6	2	8.15	67.2	4.96	3.58	80	116	14.2	1.71
	6	17	8.45	67.8	4.52	3.54	95	113	13.3	1.69
								Av.	10.9	
P. H.	2	13	6.08	63.4	3.67	2.31	73	83	13.7	1.31
	2	21	6.50	64.1	3.67	2.82	79	84	12.9	1.30
	3	0	6.80	65.5	3.76	2.63	79	85	12.5	1.30
	3	26	7.37	67.7	3.76	2.68	82	94	12.8	1.39
	5	0	8.50	71.2	3.93	3.90	108	110	12.9	1.53
	5	8	8.82	72.0	3.93	3.75	112	106	11.9	1.49
	6	0	9.30	73.5	3.93	4.00	117	118	12.6	1.60
	7	0	9.60	75.2	3.93	3.43	111	122	12.7	1.62
	7	8	9.80	75.6	3.96	4.19	123	128	12.7	1.69
	7	21	9.95	76.3	4.54	3.90	112	126	12.9	1.65
								Av.	12.7	

J. M., at 1 month and 28 days; the largest amount, 128 mg., was excreted by P. H. at 7 months and 8 days. There appeared to be no relation between the excretion of uric acid and that of creatinine. E. M., at 2 months and 8 days, put out 66 mg. of creatinine and 71 mg of uric acid; whereas J. M., at 1 month and 28 days, excreted slightly less creatinine (63 mg.) and considerably less uric acid (42 mg.). As the infants grew older, this disparity between the amount of creatinine and the amount of uric acid excreted was still extant, although not in the same proportion. At the same level of creatinine, 85 mg., two infants excreted 83 and 116 mg. of uric acid, respectively; whereas

6. Benedict, S. R., and Franke, E.: J. Biol. Chem. **52**: 387, 1922.

the third infant with a slightly lower output of creatinine (82 mg.) excreted 95 mg. of uric acid.

The amounts of uric acid excreted per kilogram of body weight by the infants in the present investigation ranged from 7.8 to 14.6 mg., with an average of 11.9 mg. These values are considerably lower than those reported by Rougichitch,[2] who found from 13.8 to 25 mg. per kilogram among a group of hospital patients suffering from various nutritional disturbances and physical defects. Even among a group of very young normal infants, the output of uric acid, in general, ran higher than our figures.[5] It seemed possible that the difference in

TABLE 2.—*A Comparison of the Amounts of Uric Acid Excreted in Infants According to the Actual and Theoretical Weights*

Present Investigation							Rougichitch[2]						
Age		Weight		Uric Acid, Mg.	Uric Acid Excreted per Kg.		Age, Months	Weight		Uric Acid, Mg.	Uric Acid Excreted per Kg.		
Months	Days	Actual, Gm.	Theoretical, Gm.		Actual, Mg.	Theoretical, Mg.		Actual, Gm.	Theoretical, Gm.		Actual, Mg.	Theoretical, Mg.	Admitted For
2	..	5,400	4,080	42	7.8	10.3	2	2,606	4,080	55	21.2	13.6	Prematurity
2	8	5,450	4,175	71	13.1	16.8	..	.....	.....	62	23.8	15.2	
2	13	6,080	4,370	83	13.7	19.0	2	3,800	4,080	59	15.4	14.4	Prematurity
3	..	6,000	4,675	48	7.9	10.3	..	.....	.....	...	....	....	
3	..	6,800	4,675	85	12.5	18.3	3	5,200	4,675	83	12.5	17.9	Normal[5]
5	..	8,500	5,880	110	12.9	18.6	5	3,800	5,880	62	16.7	10.5	Regulation of feeding
5	6	7,600	5,995	90	11.9	15.1	..	.....	.....	65	17.1	11.0	
..	..	.....	.....	...	....	....	5	4,394	5,880	110	25.0	18.7	Otitis
5	8	8,820	6,025	106	11.9	17.6	..	.....	.....	106	24.2	18.1	
..	..	.....	.....	...	....	....	5	4,764	5,880	82	17.1	13.8	Otitis
..	..	.....	.....	...	....	....	..	.....	.....	88	18.5	15.0	
6	..	9,300	6,480	117	12.6	17.8	6	5,952	6,480	129	22.8	19.9	Acute gastro-intestinal disturbance
6	2	8,150	.....	116	14.2	17.9	..	.....	.....	136	21.6	20.9	
7	..	9,600	6,680	122	12.7	18.3	7	7,037	6,680	112	16.0	16.8	Otitis

amount of uric acid eliminated per kilogram between these groups of infants might be due to the fact that some of the infants in Rougichitch's study were considerably underweight, whereas ours were overweight. We therefore estimated the amounts of uric acid excreted by the infants of the same relative ages in both groups on the basis of their theoretic weights, assuming the birth weights to have been 7 pounds (3.2 Kg.). A comparison of the figures (table 2) shows that the elimination of uric acid at the same age level in the two groups is fairly comparable. It would seem, therefore, that there is no inherent relation between body weight and the amount of uric acid eliminated, nor does the nutritional condition of the infant appear to bear any relation to the elimination of uric acid.

Since the diet of the infants consisted almost exclusively of milk, it seemed possible that the elimination of high amounts of uric acid in comparison with the amounts eliminated in adults may be, in part, the result of the ingestion of purine nitrogen in milk, which, according to a number of investigators, contains appreciable amounts. Burian and Schur [7] reported from 4.12 to 6.40 mg. of purine nitrogen in 1 liter of cow's milk, whereas Denis and Minot [8] found 15 mg. The values for human milk were considerably higher, averaging between 17 and 44 mg. per liter. In view of these observations, it does not seem probable that the excretion of uric acid of the infants under observation was materially influenced by the purine nitrogen ingested. The daily amount of milk ingested ranged from 600 to 850 cc. On the basis of the observations of Denis and Minot, P. H., who at 7 months 21 days was receiving 850 cc. of milk, was ingesting 12.5 mg. of uric acid, an amount too small to account for the large amount of uric acid eliminated (126 mg.).

Nor does the twenty-four hour excretion of uric acid of the infants studied appear to have been materially influenced by the ingestion of protein. E. M., with an intake of nitrogen of 3.3 Gm. at 4 months 7 days, excreted 83 mg. of uric acid; one week later, with an intake of 4.09 Gm. of nitrogen he excreted 83 mg. of uric acid. Similarly, J. M., at 5 months 21 days, with an ingestion of 2.21 Gm., excreted 114 mg. of uric acid; whereas at 6 months 2 days, with an ingestion of 4.98 Gm. of nitrogen he excreted 116 mg. of uric acid. P. H. excreted 128 mg. of uric acid following an intake of 3.93 Gm. of nitrogen. That the ingestion of protein is not a significant factor in the production of urinary uric acid in infants seems to be further indicated by the uric acid output of P. H. During five successive periods of study of his metabolism extending over two months, the amount of nitrogen ingested remained constant; whereas the amount of uric acid excreted increased from 110 to 128 mg. These observations are in accord with the observations of Rougichitch [2] to the effect that in his studies the relationship of urinary nitrogen to uric acid was not close, the uric acid nitrogen ranging from 1.25 to 3.5 per cent of the total nitrogen. Zwarenstein [9] also reported recently that diets rich in protein and purine-free have little influence on the total of uric acid eliminated. It is possible, however, that the effect of an increase in the ingestion of protein, which, according to Taylor and Rose,[10] Lewis and Doisy [11] and

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7. Burian, R., and Schur, H.: Ztschr. f. physiol. Chem. **23**:55, 1927; cited by Rose, W. C.: Physiol. Rev. **3**: 544, 1923.
8. Denis, W., and Minot, A. S.: J. Biol. Chem. **38**: 353, 1919.
9. Zwarenstein, H.: Biochem. J. **22**:307, 1928.
10. Taylor, A. E., and Rose, W. C.: J. Biol. Chem. **18**:519, 1914.
11. Lewis, H. B., and Doisy, E. A.: J. Biol. Chem. **36**: 1, 1918

others [12] stimulates cellular metabolism with the resulting increase in the elimination of uric acid, may not have been observed in the investigations with infants because of the fact that the eliminations of uric acid were determined only in infants who had become adjusted physiologically to the change in the level of protein. Rose observed that the "maximum effect upon uric acid excretion produced by an increase in protein consumption, usually manifests itself upon the first day after the inauguration of the dietary change, and in some cases is followed by a tendency to return to a lower level of elimination with continued use of the high protein ration." [13]

The variations in the ingestion of carbohydrate at the different food levels seem to be too small to influence the elimination of uric acid in the infants studied. To each twenty-four hour feeding mixture there was added, in general, 60 Gm. of the carbohydrate modifier, thus making a difference of approximately 12.5 Gm. of carbohydrate between the infants receiving the smallest and those receiving the largest amount of milk. Mendel and Stehle [14] obtained only a slight increase in the excretion of uric acid following the feeding of large amounts of carbohydrate in a single dose during a fasting period. It would seem improbable, therefore, that the slight increases in carbohydrate in the feeding mixtures of our infants had any appreciable influence on the amounts of uric acid eliminated.

A recent study of the excretion of creatinine of infants seems to be in accord with the theory that the endogenous creatinine is a measure of muscle mass.[15] The endogenous uric acid, on the other hand, is believed to be, in general, a measure of the glandular tissue. A comparison of the rate of increase in the excretion of the creatinine with that in the excretion of uric acid should indicate the difference in rate of development between the muscle and the glandular tissue of a given infant. With the two infants in our series who were studied over the longer periods, the rate in the increase of uric acid was 14 mg. and 8.6 mg. per month, respectively; whereas the rate of increase of creatinine was 6.4 and 9.8 mg. With the third infant, E. M., the development of muscle indicated by the increase in the rate of excretion of creatinine, 12 mg. per month, was more rapid than that of either

12. Mendel, L. B., and Brown, E. W.: Rate of Elimination of Uric Acid in Man, J. A. M. A. **49**: 896 (Sept. 14) 1907. Lewis, H. B.; Dunn, M. S., and Doisy, E. A.: J. Biol. Chem. **36**: 9, 1918. Rose, W. C.: J. Biol. Chem. **48**: 563 and 575, 1921. Lewis, H. B., and Corley, R. C.: J. Biol. Chem. **55**: 373, 1923. Gibson, H. V., and Doisy, E. A.: J. Biol. Chem. **55**: 605, 1923. Rose, W. C., and Cook, K. G.: J. Biol. Chem. **64**: 325, 1925.

13. Rose, W. C.: J. Biol. Chem. **48**: 575, 1921.

14. Mendel, L. B., and Stehle, R. L.: J. Biol. Chem. **22**: 215, 1915.

15. Daniels, A. L., and Hejinian, L. M.: Am. J. Dis. Child. **37**: 1128, 1929.

of the other two. The glandular development of E. M., on the other hand, considered at the same age level, was fairly comparable with that of P. H., but considerably lower than that of J. M. The significance of the difference in rate of growth between the muscle and the glandular tissue, as indicated by these two endogenous catabolites, creatinine and uric acid, is not clear. More data are needed before conclusions can be drawn.

In a previous report, it was shown that there is a more definite relation between the elimination of creatinine and length than between the elimination of creatinine and weight. Comparison of the height and the daily determinations of uric acid with the weight and the elimination of uric acid of the infants studied suggests that there is a closer relationship between the former than between the latter.

SUMMARY

In a series of metabolic studies of three normal infants, it was found that although the elimination of uric acid increased with increasing age, there was no close relationship between the excretion of urinary creatinine and that of uric acid; nor was there any apparent relation between the ingestion of protein and the excretion of uric acid, which averaged 12, 10.9 and 12.7 mg. per kilogram, respectively, for the three infants under observation.

With these infants there appeared to be a closer correlation between height and the amount of uric acid excreted than between weight and the amount of uric acid excreted.

THE INFLUENCE OF ULTRAVIOLET RAYS, YEAST AND IRRADIATED YEAST ON THE SUGAR TOLERANCE OF DIABETIC CHILDREN *

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Insulin has proved to be of distinct value in the treatment of patients with diabetes mellitus, but difficulties in the mode of its administration, the danger of overdosage and the transiency of its action have tended to restrict its usefulness. This led to a search for a therapeutic agent which would act like insulin, but which would not possess the latter's disadvantages. As a result, some workers found that untraviolet rays and vitamin B are capable of producing a distinct improvement in the carbohydrate tolerance of patients with diabetes mellitus. Anderson,[1] Rothman,[2] Messerle,[3] Pincussen [4] and Block and Faber [5] noted a temporary increase in sugar tolerance as a result of exposing patients to ultraviolet rays. Most of these conclusions were based on depression in blood sugar occurring within three hours after exposure. None of them, however, pursued this study over a sufficiently long period of time to warrant definite conclusions. Burge and Wickwire [6] showed that ultraviolet irradiation of paramecia not only caused a decrease in the utilization of sugar by these cells, but destroyed insulin.

* Submitted for publication, March 23, 1929.

* From the Harry Caplin Pediatric Research Laboratory, The Jewish Hospital of Brooklyn.

1. Anderson, A.: Treatment of Diabetes Mellitus with Ultraviolet Rays, München. med. Wchnschr. **70**:1484 (Dec. 14) 1923.

2. Rothman, S.: Increase of Sugar Tolerance after Light Bath, Klin. Wchnschr. **3**:1959 (Oct. 21) 1924.

3. Messerle, N.: Effect of Quartz Light and Sunlight on Sympathetic Nervous System as Shown by Blood Sugar and Adrenalin Skin Reaction, Schweiz. med. Wchnschr. **57**:759 (Aug. 6) 1927.

4. Pincussen, L.: The Influence upon Metabolism of Carbohydrate through Irradaition (Strahlung), Ztschr. f. d. ges. exper. Med. **26**:127, 1922.

5. Block, C. E., and Faber, F.: Effect of Ultraviolet Rays on Fasting Blood Sugar of Diabetics, Am. J. Dis. Child. **30**:510, 1925.

6. Burge, N. E., and Wickwire, G. C.: The Decrease in Sugar Metabolism and Destruction of Insulin by Ultraviolet Radiation, J. Biol. Chem. **72**:827 (April) 1927.

Others [7] observed that yeast extract produced a lowering of the blood sugar. Collip [8] corroborated this and, in addition, noted that the extracts of a variety of plants acted similarly. He attributed this effect to an active insulin-like principle, and not to vitamin B. Mills [9] asserted that strikingly beneficial results followed the use of an acid-alcoholic extract of plants rich in vitamin B and ascribed this action solely to the vitamin B. Stucky,[10] however, was unable to demonstrate the presence of vitamin B in commercial insulin.

The present communication is concerned with the effects of exposure to ultraviolet rays over a long period of time and of an intensive course of administration of vitamin B on the metabolism of carbohydrates.

MATERIAL AND METHODS

Five juvenile diabetic patients from the outpatient department, as subjects for this study, were divided into three groups. The first group was treated with ultraviolet rays, the second with irradiated brewer's yeast [11] and the third with yeast-vitamin concentrate.[11] Weekly records were kept for each, covering diets, insulin dosages, urinary excretions of dextrose and the determinations of blood sugar during fasting. Tests of sugar tolerance following the administration of 50 Gm. of sugar by mouth were performed before the institution of the respective treatments and at weekly intervals thereafter. The blood sugar was determined by the Kramer-Gittelman [12] micro-modification of the Folin-Wu [13] method.

GROUP 1.—Three of the subjects were exposed daily to ultraviolet radiation from a carbon arc lamp. The potency of the lamp was tested spectrophotometrically and by antirachitic effect. The period of treatment in the case of two patients (H. P. and Y. K.) was five weeks and in the case of one patient (B. L.) seven weeks. The time of exposure at the beginning was three minutes, and this was progressively increased to fifteen minutes. The distance between the lamp and the patient was maintained constantly at 20 inches (50.8 cm.). H. P. and Y. K. received their customary doses of insulin, while B. L. was under dietetic management without insulin. The results are given in tables 1 and 4.

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7. Funk, C., and von Shönborn, E.: The Influence of a Vitamine-Free Diet on the Carbohydrate Metabolism, J. Physiol. **48**:328, 1914. Winter, L. B., and Smith, W.: Problems of Diabetes Mellitus, Brit. M. J. **1**:711 (April 28) 1923. Funk, C.; Harrow, B., and Paton, J. B.: Extraction of Vitamins from Yeast and Rice Polishings Using Various Watermiscible Solvents, Proc. Soc. Exper. Biol. & Med. **20**:423, 1923.

8. Collip, J. B.: Glucokinin: A New Hormone Present in Plant Tissue, J. Biol. Chem. **56**:513 (June) 1923.

9. Mills, C. A.: Treatment of Diabetes with an Acid-Alcoholic Extract of Plants Rich in Vitamin B, Am. J. M. Sc. **175**:3, 376.

10. Stucky, C. J.: Does Commercial Insulin Contain What Has, Hitherto, Been Called Vitamin B? Arch. Int. Med. **42**:780 (Nov.) 1928.

11. The yeast was supplied through the courtesy of The Harris Laboratories, Tuckahoe, New York.

12. Kramer, B., and Gittelman, I. F.: Technic for Quantitative Estimation of Sugar in Very Small Amounts of Blood, J. A. M. A. **81**:1171 (Oct. 6) 1923.

13. Folin, O., and Wu, H.: System of Blood Analysis, J. Biol. Chem. **41**:367, 1920.

Group 2.—Two patients, I. C. and S. C., were given 10 Gm. of irradiated brewer's yeast daily over a period of seven weeks and six weeks, respectively. The finely pulverized yeast was spread in a thin layer (about 1 mm. thick) over a tray and irradiated for one-half hour at a distance of 20 inches. The admin-

Table 1.—*Effect of Ultraviolet Rays on Dextrose-Tolerance in Children with Diabetes*

		Dextrose-Tolerance Values				
		Blood Sugar During Fasting	Blood Sugar Following Intake of 50 Gm. of Dextrose			
Child	Date		½ Hour	1 Hour	2 Hours	3 Hours
		Mg.	Mg.	Mg.	Mg.	Mg.
H. P.	5/ 8/28*	322.0	406.1	525.4	467.8	396.1
	5/15/28	325.0	627.2	669.2	542.6	529.3
	5/22/28	383.3	483.6	622.8	548.0	557.0
	5/29/28	312.7	490.2	396.7	409.5	295.5
	6/ 5/28	281.6	522.7	606.7	644.0	529.6
	6/12/28	166.3	462.8	558.9	485.3	479.4
Y. K.	4/27/28*	163.9	206.2	210.0	465.0	407.2
	5/ 5/28	154.8	250.9	263.0	268.3	261.9
	5/11/28	246.2	335.4	345.3	458.5	388.5
	5/18/28	177.0	261.3	415.9	494.7	456.0
	5/25/28	91.0	156.4	441.0	389.5	274.0
	6/ 1/28	102.5	213.7	284.7	354.7	326.0
B. L.	4/12/28*	229.0	534.0	695.0	564.0	556.0
	4/20/28	209.0	308.0	339.0	400.0	324.0
	4/27/28	232.2	440.3	477.2	361.7	331.3
	5/ 5/28	173.3	303.4	398.4	351.5	296.3
	5/11/28	246.8	410.7	483.0	399.0	326.0
	5/18/28	231.0	411.9	518.0	511.0	337.2
	5/25/28	193.5	331.5	402.5	392.0	287.5

* Control

Table 2.—*Effect of Irradiated Yeast on Dextrose-Tolerance of Children with Diabetes*

		Dextrose-Tolerance Values				
		Blood Sugar During Fasting	Blood Sugar Following Intake of 50 Gm. of Dextrose			
Child	Date		½ Hour	1 Hour	2 Hours	3 Hours
		Mg.	Mg.	Mg.	Mg.	Mg.
I. C.	5/ 1/28*	148.2	250.0	448.0	412.9	312.7
	5/ 8/28	102.1	251.3	358.5	406.0	248.7
	5/15/28	308.0	342.0	351.2	350.0	329.7
	5/22/28	266.0	425.7	610.0	461.9	305.3
	5/29/28	301.0	420.0	403.7	455.5	442.2
S. C.	5/ 1/28*	256.7	451.0	518.0	544.9	336.7
	5/ 8/28	202.4	298.7	512.4	520.3	476.0
	5/15/28	289.3	330.2	485.3	567.0	567.0
	5/22/28	317.0	587.8	548.0	557.0	536.9
	5/29/28	305.7	527.3	550.8	490.0	321.5
	6/ 5/28	168.7	359.4	423.3	597.3	430.5

* Control

istration of this supposedly is equivalent to giving the patient the combined benefits of ultraviolet rays and vitamin B. The results are given in tables 2 and 4.

Group 3.—Two patients from group 1 (Y. K. and B. L.) and two from group 2 (S. C. and I. C.), after the completion of the studies mentioned, were selected for an investigation of the effect of vitamin B. They were each given 1.8 Gm. of brewer's yeast vitamin B concentrate daily over a period of six weeks. The results are given in tables 3 and 4.

TABLE 3.—*Effect of Vitamin B Concentrate on Dextrose-Tolerance of Children with Diabetes*

Child	Date	Dextrose-Tolerance Values: Blood Sugar During Fasting Mg.	Blood Sugar Following Intake of 50 Gm. of Dextrose: ½ Hour Mg.	1 Hour Mg.	2 Hours Mg.	3 Hours Mg.
Y. K.	6/ 1/28*	102.5	213.7	284.7	354.7	326.0
	6/ 7/28	115.6	179.1	285.9	374.6	446.7
	6/22/28	158.5	232.0	361.2	370.0	378.0
	7/24/28	250.0	317.3	449.1	567.0	502.0
S. C.	6/ 5/28*	168.7	359.4	423.3	507.3	430.5
	6/22/28	174.2	218.0	361.6	416.4	488.6
	7/16/28	192.9	323.8	445.6	644.0	441.0
I. C.	5/29/28*	301.0	420.0	403.7	455.5	442.2
	6/ 5/28	148.0	436.3	476.5	567.4	490.0
	6/26/28	193.8	351.2	464.7	504.8	487.7
B. L.	6/ 1/28*	172.7	434.5	445.0	314.9	317.4
	6/ 7/28	180.0	391.0	415.4	380.4	332.0
	6/22/28	218.6	296.2	354.8	401.3	315.6
	7/16/28	178.0	368.7	511.0	402.5	298.6

* Control

TABLE 4.—*Summary of the Data Pertaining to Sugar Tolerance of Children with Diabetes During the Period of Treatment and During Two Months Prior to and Two Months after the Institution of Treatment*

Child	Period of Observation	Length of Period, with Kind of Treatment	Average Amount of Available Dextrose in Diet, Gm.	Average Amount of Dextrose Excreted, Gm.	Average Amount of Dextrose Consumed,* Gm.	Average Dose of Insulin, Gm.	Dextrose Insulin Quotient†	Weight, Pounds
H. P.	Before treatment	One month	127	34.8	92.2	30	3.0	104.0
		Second month	102	13.0	89.0	35	2.5	103.0
	During treatment	Five weeks (radiation)	106	38.0	68.0	31	2.2	101.0
	After treatment	First month	117	31.0	86.0	37	2.3	102.0
		Second month	112	25.0	87.0	35	2.4	
Y. K.	Before treatment	One month	122	2.1	119.9	13	9.1	54.25
		Second month	118	13.0	105.0	18	5.8	53.0
	During treatment	Six weeks (radiation)	128	8.2	119.8	15	7.9	53.0
		Seven weeks (vitamin B)	122	9.6	112.4	13	8.6	53.0
	After treatment	First month	127	3.5	123.5	20	6.1	53.0
		Second month	124	2.6	121.4	21	5.7	53.75
B. L.	Before treatment	Five weeks	114	0.25	113.75	..	...	72.0
		Three weeks	177	35.0	142.0	..	...	75.0
	During treatment	Eight weeks (radiation)	178	49.2	128.8	..	...	76.0
		Six weeks (vitamin B)	164	53.3	110.7	..	...	76.0
	After treatment	First month	155	26.1	128.9	10	12.9	78.0
		Second month	152	8.1	143.9	13	11.0	81.0
I. C.	Before treatment	One month	141	27.7	113.3	43	2.6	57.5
		Second month	135	31.0	104.0	42	2.5	58.5
	During treatment	Seven weeks (irradiated yeast)	125	27.2	97.8	40	2.4	58.0
	After treatment	First month	168	22.1	145.9	40	3.6	55.5
		Second month	164	58.8	105.2	40	2.4	57.0
S. C.	Before treatment	One month	162	44.0	118.0	18	6.5	52.75
		Second month	167	11.3	155.7	18	8.7	53.5
	During treatment	Six weeks (irradiated yeast)	160	26.0	134.0	18	7.4	53.25
	After treatment	First month	169	14.9	154.0	25	6.3	52.75
		Second month	169	20.3	148.7	26	5.7	53.0

* Obtained as the difference between the amount of available dextrose in the diet and the amount of dextrose excreted.

† The ratio of the average amount of dextrose consumed and the average dose of insulin.

RESULTS

Table 1 represents the results of the sugar tolerance tests of the children exposed to ultraviolet rays; table 2, of two patients who received irradiated yeast; and table 3, of four patients who were given brewer's yeast vitamin B concentrate. The results in the three groups yield no clear evidence of a definite diminution in the blood sugar as determined during fasting, of a lowering in the peak or of any change in the decline of the curve during the absorption period.

Table 4 is a summary of the essential data on the five children under observation; it includes for each a record of the average amount of available dextrose in the diet, and the average of dextrose excreted. The difference between these two figures represents the average amount of dextrose consumed. There is also a record of the average insulin dosage. These averages were obtained on weekly determinations over periods of from one to two months. The ratio of the amount of dextrose consumed to the amount of insulin administered gives a quotient which has been found to be a satisfactory measure of the patient's tolerance of dextrose. It may be observed, therefore, from table 4, that the dextrose-insulin quotient remained constant during the preexperimental period of two months, during the experiment and for two months thereafter. In spite of the wide difference in the sugar tolerance curves, the dextrose-insulin quotient nevertheless was constant. The significance of the dextrose-insulin quotient, i.e., its reliability as a measure of sugar tolerance in diabetes, is discussed in a communication now in press.[14]

CONCLUSION

Ultraviolet rays, yeast vitamin B and irradiated yeast, when administered over a period of from four to seven weeks, fail to produce any significant improvement in the sugar tolerance of children with diabetes.

14. Collens, W., and Grayzel, H. G.: Treatment of the Ambulatory Juvenile Diabetic; to be published.

RELATIONSHIP OF JAUNDICE AND WEIGHT TO BLOOD VALUES IN THE NEW-BORN INFANT*

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The high hemoglobin content of the blood of the infant at birth as compared with the average value in adults, and its rapid decrease during the early days of life were first recorded by Leichtenstern.[1] His observation was amply substantiated by the work of numerous investigators who also showed that the same holds true for the erythrocyte count. The observations of a number of these writers are recorded in table 1. This list is not exhaustive, but includes the more frequently quoted figures of earlier authors and those of the more recent ones whose work covers the period from birth to the tenth day of life.

There is a wide variation in the figures quoted, and their absolute accuracy is doubtful if judged by a present day standard of values. The relative accuracy within each series, however, is probably high, and the uniformity with which they show a considerable loss of erythrocytes and hemoglobin during the first ten days of life is noteworthy.

In the time of its appearance and greatest intensity, jaundice of the new-born follows closely the period of greatest loss of erythrocytes and hemoglobin by the infant. In the light of evidence pointing to the hematogenous origin of this form of jaundice, a possible correlation between these two factors at once presents itself. Heimann,[2] in a comparison of fifty jaundiced and fifty nonjaundiced new-born infants, found that not only was the average hemoglobin value lower in the jaundiced group but it was reduced in proportion to the intensity of the jaundice. Thus, for the control group he reported a hemoglobin value of 113 per cent, against 102 per cent for the mildly, 101 per cent for the moderately and 93 per cent for the severely jaundiced infants. He made similar observations in the erythrocyte count.

Lucas[3] and his co-workers failed to verify these results. They wrote, "Heimann states that the hemoglobin of jaundiced infants is distinctly lower than that of normal infants. We have not been able

* Submitted for publication, April 20, 1929.

* From the Department of Pediatrics and the William Pepper Laboratory, School of Medicine, University of Pennsylvania.

1. Leichtenstern, O.: Untersuchungen über den Hämoglobulingehalt des Blutes in gesunden und kranken Zustanden, Leipsig, 1878.

2. Heimann, F.: Zur Lehre des Ikterus neonatorum, Ztschr. f. Geburtsh. u. Gynäk. **69**:165, 1911.

3. Lucas, W. P.; Dearing, B. F.; Hoobler, H. R.; Cox, A.; Jones, M. R., and Smyth, F. S.: Blood Studies in the New-Born, Am. J. Dis. Child. **22**:525 (Dec.) 1921.

to demonstrate this as the hemoglobin in some of our most markedly jaundiced infants was just as high as in infants without jaundice." Again referring to the erythrocyte count, "Heimann found values lower in icteric babies than in those free from icterus, 5,500,000 as compared with 6,500,000. This we were unable to substantiate."

TABLE 1.—*Blood Values in New-Born Infants*

		Erythrocyte Count				Hemoglobin, per Cent					
Author	Cases	Day	Average	Minimum	Maximum	Method	Number	Day	Average	Minimum	Maximum
Schiff: Jahrb. f. Kinderh. **34**: 159, 1892	18	1 3 7 10	7.179 7.650 6.750 6.500	5.824 6.653 6.071 5.115	7.978 8,940 8.637 8.288						
Elder and Hutchinson: Edinburgh M. J. **41**: 105, 1905	6	1	5.346	4.100	6.750	Gower	9	1	105	95	115
Aitken: J. Obst. & Gynæc. Brit. Emp. **1**: 414, 1902	32	1 3 10	7.676 7.684 5.808	6.800 4.900	8.600 7.000	Gower	22	1 10	106 105	98 95	120 115
Fehrson: J. Physiol. **30**: 322, 1903	40 37	1 10	6.045 5.516	4.300 4.200	7.250 6.592	Oliver	..	1 10	113 106	94 102	125 120
Perlin: Jahrb. f. Kinderh. **58**: 549, 1903	..	1-3	.....	5.280	7.550	.....	..	1-3	116-119		
Takasu: Arch. f. Kinderh. **39**: 436, 1904	..	1-3 4-11	4.843 4.656	3.304 3.812	6.240 5.970	Gower	..	1-3 4-10	130 121	103 98	160 140
Heimann: Ztschr. f. Geburtsh. u. Gynäk. **69**: 165, 1911	100	3 6 9	6.500 5.950 5.400	.....	.....	.....	100	3 6 9	108 103 100		
Williamson: Arch. Int. Med. **18**: 505, 1916	..	..	.....	.....	.....	Huefner	31	1 2-3 4-8 9-13	23.1 22.8 22.1 21.2	21.2 21.8 20.2 19.8	25.3 24.7 23.5 23.8*
Appleton: J. Biol. Chem. **34**: 369 1918	..	..	.....	.....	.....	Palmer & Van Slyke	12 14 14 8	1 2-3 4-8 9-13	164 146 135 137		
Slawik: Ztschr. f. Kinderh. **25**: 212, 1920	82	1 10	5.850	5.200 5.200	8.000 6.300						
Lucas et al.: Am. J. Dis. Child. **22**: 525, 1921	31 25 16 13	1 3 7 10	5.511 5.244 5.108 4.130	4.000 4.000 3.800 2.800	6.700 6.200 6.000 5.600	Palmer (modified)	32	1 2 7 10	117 114 109 97	85 95 75 70	140 130 125 120
Mayers: Arch. Int. Med. **30**: 478, 1922	41 10	1 2-14	7.630 6.260	5.060	9.610	.....	..	1 2-3 4-8 7-13	23.2 22.7 22.0 21.3*		
Silvette: J. Lab. & Clin. Med. **13**: 245, 1927	30	1	4.519	3.280	5.700	Newcomer	20	1	93	71	110
Sanford: Am. J. Dis. Child. **35**: 9, 1928	200	1 3 7 10	5.800 5.200 5.200 4.500	4.200 4.000 4.400 4.000	8.000 7.600 6.500 6.000	Palmer	..	1 3 7 10	115 105 100 94	88 82 80 66	140 135 125 120

*Grams per hundred cubic centimeters.

Lippmann,[4] in a study of the blood of the infant confined to the first forty-eight hours of life, found no change from the general observations in five who were noted as jaundiced.

4. Lippmann, H. S.: A Morphologic and Quantitative Study of the Blood Corpuscles in the New-Born Period, Am. J. Dis. Child. **27**:473 (May) 1924.

Both Heimann and Lucas apparently confined their comparisons to absolute values. It is conceivable, however, that even in the absence of absolutely lower erythrocyte and hemoglobin values for a jaundiced group as compared with a nonjaundiced group, a correlation might still exist between the loss of erythrocytes and hemoglobin between birth and the tenth day of life and the presence and intensity of jaundice during the same period.

The present work was undertaken in an effort to establish the presence or absence of such a definite relationship.

TECHNIC

The observations are based on a series of sixty-nine new-born infants. The cases were chosen on the basis of age in hours at the time of the first determination, from 8 to 12 hours being taken as the optimum. Premature infants, those showing cyanosis of the hands or feet, and those who had been delivered after unusually difficult labor were excluded. During part of the work, determinations were completed on only those infants in whom marked jaundice developed, in order that the relative number of these in the series might be increased.

Determinations were made at the same hour each day, just after the 9 a. m. feeding, on the first, third, seventh and tenth days of life. The skin of the heel was thoroughly cleansed with alcohol and dried with sterile gauze. Blood was then obtained by double incision of sufficient depth to ensure free bleeding without pressure.

Erythrocyte diluting pipets, the double chamber Neubauer blood counting chamber and cover-slips certified by the United States Bureau of Standards were used. The first drops of blood from the heel were discarded. Pipets were thoroughly shaken immediately and at frequent intervals thereafter until the count was made, which was always within an hour. Counting chamber and cover slips were cleansed with ether and wiped dry with high grade linen before each count. Both sides of the chamber were filled evenly and 160 small squares were counted under high power. Counts in which any of the five 0.04 c.mm. squares varied by more than 25 and the two sides of the chamber by more than 30 were discarded.

For the determination of the hemoglobin content a Sahli hemoglobinometer with a glass rod standard was used.[5] For this standard a curve of corrections was made based on oxygen determinations, 100 per cent hemoglobin being considered as equaling 18.5 per cent by volume. Final dilutions of the samples were made one hour after collection of the blood. All diluting tubes were calibrated to a uniform standard. In cases in which there was a reading of 140 per cent or over the tests were repeated, 10 instead of 20 mm. of blood being used.

Estimation of the cell volume was made by means of Van Allen[6] hematocrit tubes. Sodium oxalate (1 per cent) was used as diluent. Tubes were centrifugated at approximately 2,500 revolutions per minute for thirty minutes, a constant load being used.[7] A number of samples were recentrifugated for ten minutes,

5. Muller, Oskar: Ueber entheitliche Hämoglobinbestimmung mit dem Glasstabhämometer nach Sahli-Leitz, Zentralbl. f. inn. Med. **46**:50, 1925.

6. Van Allen, C. M.: An Hematocrit Method, J. A. M. A. **84**:202 (Jan. 17) 1925.

7. A size 1, type SB, centrifuge from the International Instrument Company was used and run at a speed of 13.

but as no difference in first and second readings was observed, this was not adopted as a routine. Readings were made at the erythrocyte level.

Estimation of the intensity of jaundice was made by clinical examination of the sclerae. For purposes of classification, jaundice was recorded as absent, mild, moderate or marked. I felt confidence in my ability to make an accurate classification on the foregoing basis, since I previously made similar observations on more than 300 infants, in 43 of whom the estimate was checked by van den Bergh determinations. Dependence on the sclerae obviates the difficulties of coloring otherwise encountered in a cosmopolitan clinic, particularly one in which there is a considerable proportion of negro infants. While classifying certain infants as showing no jaundice, it is fully conceded that jaundice is probably due to some process operative in all babies and that its clinical presence or absence is merely an expression of degree. By "jaundice absent" is meant, then, those infants in whom the process does not reveal itself by discoloration of the sclerae.

RESULTS AND COMMENT

For the entire series the number of erythrocytes and the hemoglobin content (table 2) agree closely with the results of Lucas [8] and Sanford.[8] The average loss of 727,000 erythrocytes and 14 per cent hemoglobin

TABLE 2.—*Blood Values in Sixty-Nine New-Born Infants*

Day of Life	Erythrocyte Count			Hemoglobin, per Cent			Cell Volume, per Cent			Weight, Gm.
	Average	Minimum	Maximum	Average	Minimum	Maximum	Average	Minimum	Maximum	
1	5,676,000	4,115,000	8,230,000	120	89	152	62.0	44.0	79.0	3,335
3	5,273,000	3,670,000	6,315,000	114	87	154	61.0	40.0	77.0	3,100
7	5,128,000	3,750,000	5,910,000	111	76	148	56.5	39.5	69.5	.....
10	4,949,000	3,260,000	5,910,000	106	74	138	51.5	34.0	67.5	3,397

between the first and tenth day of life, however, is less than that shown by these two investigators. Of the sixty-nine infants, only three failed to show loss in erythrocytes and two in hemoglobin by the tenth day of life.

The average cell volume figures are in agreement with those of Lucas and Dearing [9] for new-born infants; however, they not only are absolutely higher than those accepted as the normal for adults (43 per cent by volume, Gram and Norgaard [10]) but also give a higher volume index.[11] This coincides with the statement of Guilmard [12] that the

8. Sanford, H. N.: The Effect of Ultraviolet Light on the Blood of New-Born Infants, Am. J. Dis. Child. **35**:9 (Jan.) 1928.

9. Lucas, W. P., and Dearing, B. F.: Blood Volume in Infants Estimated by the Vital Dye Method, Am. J. Dis. Child. **21**:96 (Jan.) 1921.

10. Gram, H. C., and Norgaard, A.: Relation Between Hemoglobin, Cell Count and Cell Volume in the Venous Blood of Normal Human Subjects, Arch. Int. Med. **31**:164 (Feb.) 1923.

11. Formula for volume index $\frac{\text{Percentage by volume} \times 0.1164}{\text{Millions of erythrocytes per c.mm.}}$ Calculated assuming 5,000,000 normal cells per cubic millimeter equals 42.96 per cent by volume. The volume index expresses the ratio of the mean size of the cells in the blood examined to the mean size of the cells in the blood of a normal person.

12. Guilmard, A.: Sang **1**:427, 1927.

erythrocytes of the new-born infant are larger than those of the adult, and of Silvette [13] who found that their average diameter is greater by 0.24 micron. The volume index shows a slight variation for the different days, being 1.29 on the first day, 1.33 on the third day, 1.31 on the seventh day and 1.25 on the tenth day.

The color index is likewise high, being 1.06, 1.09, 1.1 and 1.09, respectively, on the first, third, seventh and tenth days.

In table 3 the erythrocyte count and hemoglobin content of twenty-six cases without clinical jaundice are compared with twenty-seven mildly or moderately jaundiced and sixteen markedly jaundiced

TABLE 3.—*Relation of Jaundice to Blood Values*

Jaundice	No. of Cases	Day of Life 1	3	7	10
Absent *					
Erythrocytes	26	5,546,000	5,269,000	5,122,000	4,903,000
Hemoglobin	26	118%	115%	112%	106%
Cell volume	23	61.0%	59.5%	56.0%	52.5%
Weight	26	3,342 Gm.	3,102 Gm.	.....	3,457 Gm.
Slight or moderate					
Erythrocytes	27	5,828,000	5,381,000	5,160,000	5,075,000
Hemoglobin	27	122%	114%	110%	107%
Cell volume	17	62.5%	63.0%	55.0%	51.0%
Weight	27	3,546 Gm.	3,303 Gm.	.....	3,546 Gm.
Marked					
Erythrocytes	16	5,631,000	5,388,000	5,176,000	4,812,000
Hemoglobin	16	121%	118%	112%	106%
Cell volume	10	63.0%	59.5%	58.0%	54.0%
Weight	16	2,965 Gm.	2,752 Gm.	.....	2,988 Gm.

* That is, no discoloration of sclerae.

TABLE 4.—*Relation of Jaundice to Loss in Blood Values and Weight Between First and Tenth Days of Life*

Jaundice	No. of Cases	Loss in Erythrocytes	Loss in Hemoglobin, per Cent	Loss in Cell Volume, per Cent	Gain of Weight Gm.
Absent	26	643,000	12	8.5	115
Slight or moderate	27	753,000	15	11.0	38
Marked	16	819,000	15	9.0	23

cases. The difference between the groups on each day is so slight as to be within the limits of error.

While the infants with jaundice do show a greater loss in erythrocytes and hemoglobin between the first and tenth days, than those without jaundice (table 4), the difference is slight.

It has been asserted by some that the gain and loss in weight to which an infant is subject during the first days of life represents, in the main, differences in the water content of the tissues. If this is true and the amount of water in the tissues has any effect on the percentage by volume of the blood plasma, as has also been maintained, we would

13. Silvette, H.: A Study of Erythrocyte Diameters in the Newborn, J. Lab. & Clin. Med. **13**:245, 1927.

expect those infants who lose weight from birth to the tenth day of life to have a relatively concentrated blood and accordingly show an appreciably smaller loss in erythrocytes during the corresponding period. That this holds true only to a slight degree when cases with varying degrees of jaundice are compared is shown by table 5. Thus, infants with an average gain of 160 Gm. lost only 161,000 more erythrocytes per cubic millimeter than those infants who lost an average of 105 Gm. each. When, however, a group who gained 195 Gm. is compared with a group showing a similar intensity of jaundice but who lost 100 Gm. in weight, the difference in the average loss of red cells is 345,000 per cubic millimeter (table 5).

Since in this series sixteen markedly jaundiced infants gained an average of only 23 Gm. by the tenth day, while twenty-six infants without jaundice gained 115 Gm. each, this factor would exert a leveling influ-

TABLE 5.—*Relation of Gain and Loss in Weight to Loss of Erythrocytes*

	All Cases			Cases of Like Degree of Jaundice*		
	No. of Cases	Average Gain or Loss Gm.	Average Loss in Red Blood Cells per C.Mm.	No. of Cases	Average Gain or Loss Gm.	Average Loss in Red Blood Cells per C.Mm.
Gain over birth weight on tenth day.....	45	+160	806,000	30	+195	800,000
Loss below birth weight on tenth day.....	24	—105	645,000	14	—100	455,000

* An equal number of cases in which jaundice was absent and slight is included in each group.

ence when the loss of erythrocytes between a jaundiced and nonjaundiced group is compared.

Lepine [14] and Hayem [14] first advanced the theory that changes in the erythrocyte count per cubic millimeter in new-born infants were apparent only and were brought about by variations in the quantity of blood plasma. After Cohnstein [14] and Zuntz [14] offered some experimental proof for this in animals, the view was adopted by a number of writers including Knöpfelmacher [14] and Frank.[15]

A marked increase in plasma volume would be necessary to cause the loss of red cells so consistently found in new-born infants. Such an increase has yet to be demonstrated. On the contrary, the work of Bakwin [16] using the serum protein content of the blood as an index

14. Quoted by Knöpfelmacher, W., in Pfaundler and Schlossman: The Diseases of Children, Philadelphia, J. B. Lippincott Company, 1908, vol. 2, p. 24.

15. Frank, M.: Beiträge zur Biologie der weissen Blutzellen in der Neugeburtsheit und im Saüglingsalter, Ztschr. f. Kinderh. **31**:16, 1921.

16. Bakwin, H.: Dehydration in New-Borns, Am. J. Dis. Child. **24**:497 (Dec.) 1922; Dehydration Fever in New-Borns, ibid. **24**:508 (Dec.) 1922.

would indicate a decrease in plasma water during the first three or four days of life, followed by a return to approximately the former level. Later, Bakwin and Rivkin [17] showed that there is an abrupt fall in the volume of red cells during the first weeks of life, the curve for corpuscular volume running in general parallel to that of the total blood volume; this indicated that the fall in red cell count and hemoglobin percentage during this period is due to an actual reduction in the number of circulating corpuscles and not to an increase in plasma volume. Their work did not, however, include determinations on babies younger than 12 days, while the figures of Lucas and Dearing [9] on infants from birth to the fifteenth day show a wide variation in the percentage of blood by volume in different individuals. After this period the variations between individuals become much less marked and are uniform for a given infant.

Repeated determinations of the blood volume on the same infant between birth and 10 days of age have not been made. The figures available would indicate that during this time the volume of the plasma does not maintain the constancy which later becomes its attribute. This is also indicated by the wide variation between minimum and maximum blood values and by the great fluctuations sometimes observed in repeated determinations. These fluctuations are not sufficient in any large series to offset the destruction of erythrocytes pointed out by their consistent fall per cubic millimeter. In infants in whom marked dehydration occurs, however, the results are considerably modified. Seven such infants showed an average gain of 22,000 erythrocytes per cubic millimeter between birth and the third day, against a loss of 403,000 for the series as a whole.

Changes in the percentage by volume of the blood plasma may be sufficient to prevent a closer correlation than shown in this series between the intensity of jaundice and the loss of erythrocytes and hemoglobin between birth and the tenth day of life.

SUMMARY

The erythrocyte count and hemoglobin content of the blood of sixty-nine infants on the first, third, seventh and tenth days of life is reported.

The percentage by volume of the cells in the blood of fifty new-born infants is also reported. The cell volume is considerably greater than the average value for adults. The volume index is also high.

17. Bakwin, H., and Rivkin, H.: The Estimation of the Volume of Blood in Normal Infants and in Infants with Severe Malnutrition, Am. J. Dis. Child. **27:** 340 (April) 1924.

Infants with jaundice do not show lower average erythrocyte and hemoglobin values than those without jaundice.

Practically all infants show a loss of erythrocytes and hemoglobin between birth and the tenth day of life. The average loss of infants with marked jaundice is only slightly greater than that of infants with no jaundice.

Relative changes in weight exert an effect on the loss of erythrocytes when the infants compared show the same degree of jaundice.

Infants with marked jaundice show a much smaller gain over their weight at birth on the tenth day of life than infants without jaundice. This exerts a leveling factor when one compares the loss of erythrocytes in the two groups.

Dehydration, when of a degree sufficient to be plainly manifest clinically and to cause fever, exerts a marked influence on the erythrocyte count.

Changes in percentage by volume in the plasma may be sufficient to prevent a closer correlation between the intensity of jaundice and the loss in erythrocytes and hemoglobin than is shown in this series.

TUBERCULOSIS IN INFANTS UNDER ONE YEAR OF AGE

A STUDY OF THE AUTOPSY AND THE CLINICAL OBSERVATIONS ON INFANTS WITH TUBERCULOUS LESIONS*

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Over a period of thirteen years at the Harriet Lane Home for Invalid Children, autopsies were performed on seventy-five infants under 1 year of age who showed tuberculous lesions. These autopsies were performed by different men in the pathological department of the Johns Hopkins Hospital, and therefore the records do not have the value which they would have if the autopsies had all been done by one person who was primarily interested in the tuberculosis of infants. The autopsy records are on the whole complete, but do not always contain positive statements of negative observations.

EXPOSURE

No history was available in two cases (2.7 per cent of the total number of cases).

A positive history of exposure occurred in twenty-five of the remaining seventy-three cases (33.3 per cent of the total number), a suggestive history in nine cases (12 per cent), and a negative history in thirty-nine cases (52 per cent). The sources of contagion are shown in table 1.

The history of exposure was not especially inquired into, and no social service worker was sent to the homes to make inquiries concerning exposure. In about half of the cases, therefore, a history of exposure was obtained, and in these the exposure was sufficiently obvious to impress itself on the mind of the person giving the history. For the thirty-three patients who had a negative history, there would have to be considered the possibility of a contact with some person in whom tuberculosis had not been diagnosed, or who had a "closed case."

Margarete Röpke [1] has shown that 40 per cent of the infants who had positive skin reactions live in contact with adults who are tuber-

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* From the Department of Diseases of Children, College of Physicians and Surgeons, Columbia University. Material obtained from the Harriet Lane Home of the Johns Hopkins Hospital, through the courtesy of the Department of Pediatrics, Johns Hopkins University School of Medicine.

1. Röpke, Margarete: Beitr. z. Klin. d. Tuberk. **54**:252, 1923.

culous but who may not show a positive sputum. This shows the danger of prolonged contact, even though the adults are supposed to have "closed cases."

Armand-Delille and Famin [2] made investigations on 173 infants with tuberculosis. One hundred and forty were found to have had definite exposures, and 33 had had contact with someone who had had tuberculous symptoms at some time. Ninety-eight per cent of these patients had had a familial contact.

TABLE 1.—*Sources of Contagion*

Source	Number of Cases
Mother	12
Father	6
Grandmother	1
Grandfather	1
Both grandparents	1
Brother	1
Aunt	1
Uncle	2

TABLE 2.—*Sources of Contagion Found by Lemaire*

Source	Number of Cases
Mother only	6
Mother and father	3
Father only	9
Grandmother	2
Relative	2
Wet-nurse	1

TABLE 3.—*Sources of Contagion Found by Parisot and Saleur*

Source	Number of Subjects Observed	Proportion per 100 Infected Subjects
Mother only	115	89
Father only	221	83
Grandparents and relatives	185	79
Servants and their families	24	85
Parents or strangers	53	94

The sources of contagion found by Lemaire [3] in twenty-five nursing infants who died of tuberculosis are given in table 2.

In only one case was the duration of contagion less than four months.

The sources of contagion found by Parisot and Saleur [4] are shown in table 3.

Calmette [5] stated that Couvelaire has shown that many infants born of tuberculous mothers and separated from them immediately after

2. Armand-Delille and Famin: J. de méd. de Paris **43**:711 (Aug.) 1924.

3. Lemaire: Rev. de la tuberc. **6**:228, 1925.

4. Parisot and Saleur: Rev. d'hyg. **48**:281 (Nov.) 1926.

birth have died without apparent cause during the first weeks of life. The proportion of deaths called "unexplained" varies from 12 to 38 per cent.

On the basis of statistics gathered in France, Sweden and England, Calmette [5] concluded that more than 24 per cent of infants who are born of tuberculous mothers, or who are brought up in surroundings in which more than one in the family has tuberculosis, succumb to a tuberculous infection during the first year of life.

By using the Pirquet skin test, Calmette [5] found that among 150 infants living in a tuberculous environment, 76 (50.6 per cent) became infected before the end of the first year.

PLACENTAL TRANSMISSION

In considering the thirty-three infants who gave a negative history, the possibility of placental transmission would have to be taken into account.

Von Reuss [6] showed a chart of twenty-four cases which he believed to be definite instances of placental transmission. This chart includes the records of four fetuses and twenty infants whose death occurred from a few hours to five months after birth. The twenty infants showed lesions of varying severity, which ranged from caseous tracheobronchial glands to caseous pneumonia in the lungs. Three fetuses showed tubercle bacilli; the fourth fetus showed miliary tubercles in the liver, spleen, peritoneum and pleura. All the mothers had tuberculosis, except one who was said to be healthy. Von Reuss made the distinction between congenital tuberculosis, by which he meant tuberculous changes in the body of the new-born child, and hereditary tuberculosis, or transmission of tubercle bacilli into the infant's circulation, which results later in tuberculous changes.

Whitman and Greene [7] described a case of a stillborn infant of nine months' gestation who showed lesions in the lungs, kidneys, spleen, pancreas and medulla. The placenta contained caseous nodules.

Gilkey [8] described a case of miliary tuberculosis in an infant, aged 28 days. The mother had had tuberculosis and had been in contact with the child.

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5. Calmette: L'infection bacillaire et la tuberculose chez l'homme et chez les animaux, Paris, Masson, 1928.

6. Von Reuss: The Diseases of the New-Born, New York, William Wood & Company, 1921, pp. 626.

7. Whitman, R. C., and Greene, L. W.: Disseminated Miliary Tuberculosis in Still-Born Fetus, Arch. Int. Med. **29**:261 (Feb.) 1922.

8. Gilkey: Arch. Pediat. **42**:600 (Sept.) 1925.

Debré and Lelong [9] expressed the belief that frank congenital tuberculosis is extremely rare, but does exist. They felt that the existence of latent congenital tuberculosis has not been proved.

Couvelaire [10] described several cases of fetuses which were born of mothers having severe tuberculosis during gestation, and who apparently were carriers of the tubercle bacillus without showing any anatomic lesions. With Calmette, Valtis and Lacomme, Couvelaire observed seven cases in which transplacental transmission seemed to be proved.

Ribadeau-Dumas [11] expressed the opinion that a mother with lesions which are becoming progressively worse during gestation can transmit bacilli to the fetus through the placenta. He believed that, besides a frank congenital tuberculosis, there occurs, probably more frequently, an "occulte" tuberculosis. This "occulte" tuberculosis is characterized by debility with progressive malnutrition, or a rapid and temporary malnutrition. This malnourished condition corresponds to a form recently recognized as a tuberculous infection caused by filtrable forms of the tubercle bacillus.

Calmette [5] felt that his work and that of Guérin, Deléarde and Prospert, and the facts gathered on the services of Marfan, Nobécourt, Lereboullet, Méry and Debré, Apert and Aviragnet, show that many infants who are born of tuberculous mothers and who die in the third or fourth month of life, either of what is called "congenital debility" or without known cause, and who do not show the least evidence of tuberculosis at autopsy, often are victims of what he calls a "tuberculous ultravirus." He believed that this is transmitted in utero through the placenta. The virulence of these organisms has been proved many times by experimental inoculation, even in cases in which the mother's tuberculosis has not seemed serious.

Dr. J. Whitridge Williams [12] of the Johns Hopkins Hospital stated that in the examination of about 35,000 placentas in his service, no instance of tuberculosis of the placenta has been found, even in the case of a woman with advanced miliary tuberculosis.

On the basis of the literature, it seems fair to conclude that congenital tuberculosis occurs, but is rare. The views of Calmette and his school, that placental transmission is common, do not seem to be founded on good evidence and are probably incorrect.

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9. Debré and Lelong: Ann. de. méd. **18**:347 (Nov.) 1925.
10. Couvelaire: Presse méd. **35**:225 (Feb.) 1927.
11. Ribadeau-Dumas: Rev. franç. de pediat. **3**:370 (July) 1927.
12. Williams, J. Whitridge: Unpublished communication.

PATHOLOGY

Nodes.—In 119 autopsies on tuberculous infants, Holt [13] found the tracheobronchial glands to be involved in 96 per cent of the cases. In 47 tuberculous children under 1 year of age, Hedren [14] found that the bronchial lymph glands were involved in 100 per cent. Comby [15] found that of 278 infants below 2 years of age with tuberculosis, 100 per cent had involvement of the mediastinal glands.

These observations of Holt, Hedren and Comby were not borne out in the series presented in this paper. In 83 per cent of the cases, the tracheal or bronchial glands were recorded as being involved. In the remaining 17 per cent, no mention of involvement of the nodes of the mediastinum is made; mention, however, is made of involvement of the mesenteric glands, enlargement and caseation being, of course, the principal manifestations. However, the fact that the bronchial lymph glands were not mentioned as giving evidence of tuberculosis does not imply that they were not involved in a microscopic sense, but intimates rather that they were not sufficiently involved macroscopically to attract any observation.

Lungs.—The lungs were involved in every patient except two. One of these two children had no lesion outside the meninges, except an involvement of the glands near the bifurcation of the trachea. The other had an involvement of only the bronchial glands and the glands near the aorta.

Miliary tubercles were present in every case in which the lungs were involved, except the three following: One child showed a caseous and gelatinous bronchopneumonia of the lower part of the lower lobes of the lungs. The spleen, liver and kidneys showed tubercles. The mediastinal and mesenteric glands were involved, the jejunum showed ulcerations, and the peritoneal surface of the ileum showed tubercles. The second child showed caseous foci of the lungs, pleural adhesions on the left side, tubercles of the spleen and liver, and an involvement of the cervical, hilar and mesenteric nodes. The third child showed caseous pneumonia of the upper and lower lobes of the left lung and of the lower lobe of the right lung, with pleural adhesions on the left side. Dr. McCallum specified that the spleen and liver in this case showed small foci of caseation, but no tubercles. The kidney, pancreas and thyroid also showed similar caseous foci.

Type and Location of Involvement of the Lungs: Two thirds of the patients had tuberculous bronchopneumonia or lobular pneumonia, nearly always caseous. This was found more often on the right side,

13. Holt: Tuberculosis in Infancy and Childhood, London, Kolynack, 1908.

14. Hedren: Ztschr. f. Hyg. u. Infektionskrankh. **73**:273, 1912.

15. Comby, J.: Traité des maladies de l'enfance, Paris, Vigot Frères, 1920.

and most frequently in the lower lobes. This site corresponds, of course, with the most frequent site of cavities.

A few cases showed nontuberculous pneumonia, bronchopneumonia, lobular pneumonia or bronchitis occurring as a terminal condition.

Infrequently, the areas of bronchopneumonia showed an encapsulation of fibrous tissue, which evidently denoted an effort on the part of the organism to limit the process, which was ineffectual on account of the involvement in other parts of the body, such as the brain or the intestines.

It is important that there was a widespread involvement in two thirds of the patients in whom pulmonary tuberculosis was present.

Three patients whose roentgenograms suggested epituberculosis were proved microscopically to have caseous pneumonia.

Cavities: Cavities occurred in nearly 50 per cent of the cases. They occurred most frequently on the right side. The lower lobe was affected in the largest percentage. The cavities varied in size from those which were just visible to one which occupied nearly the entire lung on one side. In half of the cavities, there was communication with a bronchus. Blood vessels stretched across four of the cavities. One cavity showed a definite wall of granulation tissue about it, and some older fibrous tissue. Tuberculous pneumonia in conjunction with an ordinary confluent lobular pneumonia was found in the lung which contained this cavity. On microscopic examination, another cavity showed several areas in which tubercles had extended into veins or bronchi.

Cavities were definitely diagnosed by the x-rays in only one of these cases, although in two other cases suggestive pictures were obtained.

Comby [15] found that among twenty-one infants with tuberculosis, ranging in age from 3 months to 2 years, seven had cavities which were either single or multiple and were located in the apex, the middle lobe of the right lung or the base of the lungs.

Ghon [16] found that of 191 infants in the first year, 34 per cent had cavities. He also found that the number of cavities increased in the second half of the first year. He divided cavities into two types: "primary cavities," which are cavities formed from the primary focus, and "secondary cavities," which develop as a result of a secondary infection or as a dissemination from the primary focus.

Dufourt [17] found cavities in seven of thirty-four infants on whom autopsies were performed.

In autopsies on seventy-two infants under 2 years of age, Holt [18] found thirty-five which showed cavities. These cavities varied in size

16. Ghon: Ztschr. f. Tuberk. **43**:3, 1925.

17. Dufourt: Lyon méd. **137**:449 (April 18) 1926.

18. Holt: Diseases of Infancy and Childhood, New York, D. Appleton & Company, 1910.

from that of a cherry to that of a hen's egg and were occasionally much larger.

In eleven of forty-two infants under 1 year, Stirniman [19] found cavities ranging in size from that of a pea to that of a hazel-nut. Once he found a cavity involving the whole lobe which was filled with pus. He found that the left side was more often involved than the right, and the upper lobe more often than the lower.

Ribadeau-Dumas [20] found cavities at autopsy in twenty-two of sixty-eight children varying in age from birth to 2 years.

Blumenberg [21] found that in from one third to one half (45 per cent) of his infants dying of tuberculosis in the first year, the primary focus was the origin of a cavity.

Eckstein [22] reported three types of cavities in infants in their first year: first, small cavities the size of a pea, with no fibrous encapsulation about them, which it is not possible to diagnose clinically; second, big, isolated cavities with induration or infiltration of the wall, which can sometimes be diagnosed clinically, which he found to be rare at this age, and, third, some cavities with the characteristics of both the first and the second types. Infants with the third type of cavity often showed a negative tuberculin reaction, as the process usually develops fast. Eckstein felt that it is important to make a differential diagnosis between nontuberculous, caseous pneumonia which may lead to the formation of cavities and pseudocavities which accompany an emphysema and which may go on to recovery.

Eckstein [22] believed that the clinical importance of cavities in the first year is great, as children who have them nearly always die. He stressed the point that the infant's reaction is exudative rather than fibrotic.

Péhu and Dufourt [23] reported cavities in seven of thirty-four infants under 1 year of age.

Pleurae: Pleural adhesions were present in nearly 50 per cent of the cases, occurring most frequently on the right side. A pleural effusion was present once. In this case, each pleural cavity contained about 50 cc. of a thin, watery, pale yellow fluid. On the left side, the fluid was almost clear. On the right side, there were numerous flakes of opaque, grayish-yellow, purulent material. Tuberculous pneumonia and cavity formation were also present.

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19. Stirniman: Jahrb. f. Kinderh. **11**:756 (May) 1905.

20. Ribadeau-Dumas: Bull. et mém. Soc. méd. d. hôp. de Paris **35**:548, 1913.

21. Blumenberg: Beitr. z. Klin. d. Tuberk. **62**:532, 1926.

22. Eckstein: Ztschr. f. Tuberk. **48**:97, 1927.

23. Péhu and Dufourt: La tuberculose médicale de l'enfance, Paris, Gaston Doin, 1927, p. 732.

Tubercles were occasionally present in the pleurae. Patches of caseous tuberculous material occurred infrequently in the pleurae.

In four cases in which the pleura was involved (adhesions, fluid or tubercles), tubercles were the only tuberculous involvement found in the lungs. In all the other cases in which pleural involvements occurred, there were gross tuberculous lesions in the lungs. However, in about a third of the total number of cases which showed a more or less extensive involvement of the lung, there were no pleural adhesions or fluid.

Moussous [24] emphasized the rarity of dry pleurisy and pleurisy with effusion in infants. Péhu and Dufourt [23] also emphasized the rarity of pleurisy in infants. They doubted whether it has been found more than twenty times in hundreds of observations in France and other countries. Pleurisy, or pleurisy with effusion, as a primary disease such as occurs in older children and adults is rare in infants. Pleurisy in infants in conjunction with tuberculosis of the lungs, especially when the involvement is marked, is common.

The Spleen, Liver and Kidneys.—The spleen was involved in nearly all cases, the principal lesion found being miliary tubercles. When an accessory spleen was present, tubercles were found in it also. The tubercles had become caseous in quite a number of the cases.

The largest spleen noted was one weighing 80 Gm. It occurred in a child, aged 6 months, who had general miliary tuberculosis.

Two children had spleens weighing 70 Gm. One was 9 months old and had general miliary tuberculosis, and the other was 10 months old and had tuberculous pneumonia.

Six children who showed caseous masses in the spleen had a widespread involvement.

The liver, also, was involved in nearly all the cases. The incidence of tubercles was slightly less than in the spleen. The tubercles were occasionally conglomerate. In one child, the liver showed large fresh necroses. No mention was made of a splenic involvement. This child had been ill for more than three months, and had developed tubercles and tuberculous pneumonia in the lungs, and tuberculous ulcerations in the intestines.

The kidneys showed tubercles in more than half of the total number of cases.

Tuberculous Ulceration of the Intestines.—One third of the total number of cases in this series showed a definite ulceration of the intestines. Probably the incidence was greater than a third of the cases, but no lesion was noted grossly or anatomically in more than that number.

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24. Moussous: Rev. de la Tuberc. **4**:431, 1923.

In four of the cases there was mucus, blood or pus, or all three, in the stools. In one of these four cases, an antemortem diagnosis of dysentery was made because of the presence of the Shiga organism. It is questionable whether, in tuberculous ulcerations, the stools may take on the form seen in dysentery. Such a result cannot be common, because it is rare for infants with tuberculosis to show anything abnormal in the stools. In no case was a large amount of blood found at autopsy or severe bleeding ante mortem.

There was no case of intestinal ulceration in which the mesenteric nodes were not caseous. There were, however, nearly as many cases in which the mesenteric nodes were caseous but in which there was no intestinal involvement as there were cases showing involvement of the intestines. Probably more careful search of the intestines in most of these cases would have revealed some kind of tuberculous lesion.

Hedren [14] found that of forty-seven infants under 1 year, eighteen showed tuberculosis of the intestines.

Stirniman [19] reported that of forty-two children under 1 year he found eighteen who showed an ulceration in the gastro-intestinal tract. This condition occurred twice in the stomach and sixteen times in the intestine.

In thirty-four children under 1 year, Péhu and Dufourt [23] found intestinal ulcerations present three times. They said that a patient with secondary tuberculous enteritis may clinically have two or three liquid stools which are yellow or green, or the diarrhea may be severe and simulate a real dysentery, especially if the lesions are in the large intestine. Bloody stools have been observed, which occasionally showed a condition severe enough to resemble that of melena.

Brain and Meninges.—Forty-five per cent of the infants in this series showed tuberculous meningitis at autopsy. Goodhart and Still [25] found 48 per cent of their series to have meningitis. It seems fair to conclude that the infant's organism is able for a long time to protect the meninges from becoming involved, because in such a large percentage of cases the meningitis probably did not occur until the lesions elsewhere were considerably advanced and because in more than 50 per cent of the cases it did not occur. (The brains of six children who had tuberculous meningitis were not examined at autopsy). It is probable that the general tuberculous involvement is slight only if the meningitis occurs early, and kills the patient before there has been a chance for the tuberculosis to spread throughout the body. In the cases of tuberculous meningitis in which the length of illness was approximately

25. Goodhart and Still: Diseases of Children, London, J. & A. Churchill, 1905.

known, the average duration of the illness was twenty-two days, the shortest time being eight days; whereas, the children who had involvement of the lungs as the chief lesion were ill sometimes for six months before death occurred.

Practically every child who died of tuberculous meningitis had a more or less extensive involvement of the lungs, and about half of them had cavities. The spleen and liver were practically always involved. The intestinal tract showed infection in a third of the cases. As stated already, one child who died of tuberculous meningitis had as the only other lesion a caseous involvement of the nodes at the bifurcation of the trachea. Miliary tuberculosis was present in every case of tuberculous meningitis.

It would seem more accurate to specify that an infant has tuberculous meningitis and acute general miliary tuberculosis rather than to include the meningeal involvement under the heading of acute general miliary tuberculosis. Apparently children under 1 year of age who die of tuberculous meningitis are apt to have just as much, if not more, involvement of the lungs and an equal amount of involvement in other organs as those who die from a nonmeningeal tuberculosis.

Solitary tubercles were seldom found in the central nervous system. It is now believed that they occur frequently and probably would have been found more often in this series if serial sections of the brain had been made. In the four cases in which solitary tubercles were reported, one tubercle was on the surface of the cortex and was caseous. The second of these cases showed a solitary tubercle in the cord and one in the medulla. The third showed a caseous tubercle on the inferior surface of the left frontal lobe, measuring 1 by 1 cm., and a similar tubercle on the right posterior occipital lobe. In the final case, the thalamus showed a tubercle measuring about 1 by 1 cm., and the cerebellum contained a smaller one. In three of these cases, an accompanying tuberculous meningitis was proved at autopsy. All four of these children had neurologic symptoms. The child in whose thalamus a tubercle was found on clinical examination showed a stiff neck and rigidity of the arms.

Organs Less Frequently Involved.—Peritoneum: Peritonitis occurred in five infants (6.6 per cent of the total number of cases). Adhesions and tubercles involved the omentum, bladder, tubes, ovaries and rectum in one child, aged 4 months. In another child of 7 months, the peritoneal cavity was obliterated, the intestinal loops being adherent to each other and to the abdominal wall. The peritoneal surfaces of the stomach and intestines showed tubercles. The ovary was covered with granulation tissue, and the tubes had a thickened surface with tubercles embedded in it. They were filled with a yellow, cheeselike material on section, and granulation tissue was also present.

In a third child, aged 7 months, adhesions and tubercles were present in the peritoneum, and a fourth child of 8 months showed a localized peritonitis with caseous areas in the peritoneum. Another child of 11 months showed a localized peritonitis with adhesions to the spleen. Apparently the peritonitis was plastic.

The bone-marrow is said to be a frequent site of tubercles. In this series, they were demonstrated a few times in the bone-marrow of the rib and femur. None of the infants had tuberculous osteomyelitis.

The heart showed tubercles—once on the endocardium, once on the epicardium and twice on the pericardium.

In only two children were choroidal tubercles found. One of these two had meningitis. Two other children showed serous fluid in the optic nerve, and both of these had meningitis. In another child, the sheath of the optic nerve was said to show chronic meningitis. Six cases were reported as showing normal eyes. In the remaining sixty-four patients, the eyes were apparently not examined.

CASES IN WHICH TUBERCULOSIS WAS A CHANCE OBSERVATION

One child, who died of pneumococcus septicemia and meningitis, showed tuberculous lesions in the mesenteric nodes and in those at the hilum, and miliary tubercles in the lung.

One child presented a history of diarrhea with mucus, pus and blood in the stools, and the Shiga bacillus was isolated. Therefore, the case was considered one of dysentery, but at autopsy tuberculous involvement of the nodes and tubercles in the lung, liver and spleen were found.

A child, aged 6 months, whose only clinical symptoms were an abscess of the thigh and furunculosis, accompanied by a diarrhea with blood and mucus, at autopsy showed a caseous tuberculous involvement of the bronchial nodes and of those near the aorta.

The cases in which tuberculosis was a chance observation were so few that conclusions cannot be drawn as to whether the localizations differ from those in which tuberculosis was the cause of death.

PROBABLE CAUSE OF DEATH IN CHILDREN NOT DYING OF TUBERCULOUS MENINGITIS

In about two thirds of these cases, there was sufficient involvement of the lungs to cause death. About one half of them showed more or less severe involvement of the intestines. Five children had peritonitis. Two cases showed involvement of the nodes and a general disseminated miliary process only, and death probably occurred from the toxicity caused by the wide dissemination of tubercle bacilli.

In one premature infant, aged 7 weeks, the oldest lesion was evidently an involvement of the mesenteric nodes. It was noted that there were no old lesions in the lungs, only miliary tubercles being

found. There were ulcers in the jejunum, ileum and colon, with a clinical history of frequent loose stools with mucus and blood, so presumably the child died of tuberculous enteritis.

Erysipelas was the immediate cause of death in one child who had a fairly well disseminated process.

EARLIEST AGE INCIDENCE

The age incidence in the five youngest infants is shown in table 4. The cases of the two youngest (premature infants) have already been described by Grant.[26] Doubtless the prematurity of these two infants was an important factor in their early death. There was a sufficiently widespread involvement in four of these five children to cause death without an involvement of the meninges, which occurred in only one. It is interesting to note that four had a more or less severe diarrhea as a prominent symptom, but only one had tuberculous involvement of the intestines. The infant who had dysentery (Shiga) showed no ulcers of the intestine on gross examination. It would seem that the extent of the lesions in young infants does not differ essentially from that of infants during the middle or later months of the first year. The process evidently spreads fast, owing to their lack of resistance.

DIAGNOSTIC MEASURES

Tuberculous Meningitis and Lumbar Puncture.—In all the cases of meningitis except six, the diagnosis was proved at autopsy. The brain was not examined in these six cases, but tuberculosis was found elsewhere in the body. The diagnosis was made ante mortem by a positive spinal fluid in all cases except one, in which a lumbar puncture was not done. In one case in which the fluid showed a positive Pandy test and thirty-seven cells, meningitis was not found at autopsy. In another case showing an increased pressure, a positive Pandy test and a cell count of eight, nothing of importance was found at autopsy.

Skin Tests.—Debré and Laplane [27] found that the period of incubation in infants was not shorter than two or three weeks and not longer than four months.

Table 5 shows the result of the skin tests.

Pirquet tests were done on twenty-three infants, and Mantoux tests were done on thirty-nine. Both tests were made on three. In sixteen cases, neither test was done, or else it was not read before death. There seems to be no striking difference between the number of days between the test and death in the cases showing negative and positive reactions

26. Grant, J. H. B.: Miliary Tuberculosis in Premature Children, Am. J. Dis. Child. **32**:407 (Sept.) 1926.

27. Debré and Laplane: Presse méd. **32**:101, 1924.

TABLE 4.—*Age Incidence in Five Infants Under 4 Months of Age*

Infant	Age	Exposure	Length of Illness	Clinical Symptoms	Clinical Diagnosis	Probable Mode of Death	Pathologic Changes
L. B. Premature (8 months)	7 weeks	Mother died of tuberculosis while child was in hospital	1 month	Weight on admission, 4 pounds 2 ounces (1,871 Gm.); otitis media; abscess of buttocks; stools contained mucus and blood	Miliary tuberculosis; tuberculous ulcers of intestine; otitis; abscess of buttocks	Malnutrition with severe diarrhea	Miliary tuberculosis of spleen, liver, lungs, pancreas, thyroid and kidneys; tuberculous ulcerations of jejunum, ileum, and colon; caseous mesenteric lymph nodes
E. H. Premature (7 to 7½ months)	7 weeks	Mother died of tuberculosis in same month as infant	2 weeks	Weight on admission, 3 pounds 12½ ounces (1,715 Gm.); temperature irregular, up to 103.4 F.; vomiting and loose stools	Prematurity; acute general miliary tuberculosis; tuberculous caseous pneumonia	Malnutrition with diarrhea and vomiting	Miliary tuberculosis of lungs, liver, spleen, kidneys, suprarenals, pancreas, and bone marrow of rib and femur; caseous pneumonia (left lung);* caseous mediastinal and peribronchial nodes
A. K.	3½ months	Mother has tuberculosis	15 days	Weight on admission, 5 pounds 14½ ounces (2,679 Gm.); signs in lungs; liver palpable; enlarged glands; rapid respiration; cyanosis; Pirquet and sputum negative	Pulmonary tuberculosis	Tuberculous bronchopneumonia	General miliary tuberculosis of lungs, spleen, liver, pericardium and mesentery; caseous pulmonary tuberculosis (with cavities in three lobes); tuberculous pleurisy; caseous tuberculosis of bronchial, mediastinal and abdominal lymph nodes
J. D.	3¾ months	Negative	2 months	Weight on admission, 11 pounds 1 ounce (5,017.8 Gm.); signs in lungs; palpable liver and spleen; tuberculids; meningeal signs; lumbar puncture positive; watery stools; Pirquet positive	Feeding regulation; rickets; general miliary tuberculosis; tuberculous meningitis	Tuberculous meningitis	General miliary tuberculosis of lungs, spleen, liver and kidneys; tuberculous meningitis; caseous tuberculous bronchopneumonia
W. D.	3¾ months	Undetermined	12 days	Weight on admission, 10 pounds (4,539.9 Gm.); respiration rapid with apnea and cyanosis; stools frequent and loose with mucus, pus and blood; dehydration; stool culture, B. dysenteriae Shiga	Dysentery (Shiga); acute general miliary tuberculosis (tuberculosis not suspected ante mortem)	Dysentery (Shiga)	General miliary tuberculosis of lungs, spleen and liver; caseous tuberculosis of lymph nodes

* There was a nontuberculous pneumonic process in the right lung which Dr. McCallum believed to be the effect of several organisms.

TABLE 5.—*Result of Skin Tests*

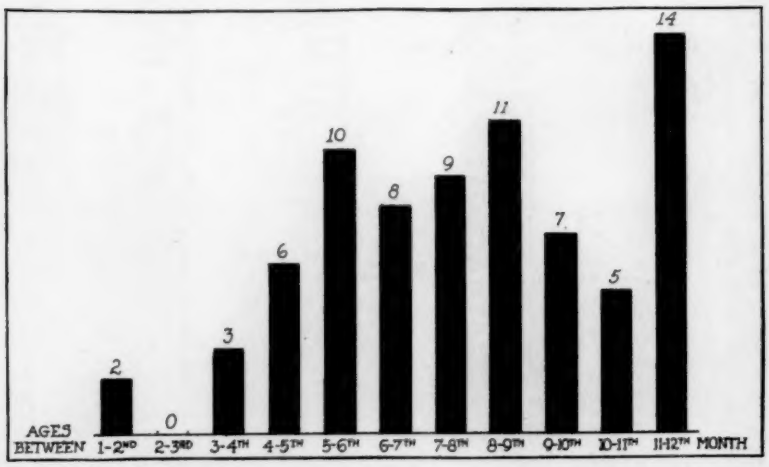
Infant	Age, Months	Pirquet Test	Mantoux Test		Other Doses	Length of Time Between Test and Death	Approximate Length of Illness
			0.1 Mg.	1 Mg.			
E. M. B.	7	.....	Negative	.....	.....	6 days	20 days
W. C.	7	.....	Negative	Negative	.....	?	?
D. H.	8	Negative	.....	.....	.....	7 days	4 months
			Neg., 0.01 mg.	.....	.....	6 days	
M. T.	5¼	.....	Negative	.....	.....	2 days	1 month
					Neg., 3 mg.	Day of death	
V. S.	9	.....	Negative	.....	.....	2 weeks	3 weeks
				Negative	.....	2½ weeks	
R. S.	6	Negative	.....	.....	.....	15 days	15 days
G. F.	8	Negative	.....	.....	.....	6 days	33 days
D. C.	4	Negative	.....	.....	.....	3 days	25 days
C. H.	9	Negative	.....	.....	.....	3 days	3 days
A. K.	3	Negative	.....	.....	.....	1 day	15 days
W. W.	8	Negative	.....	.....	.....	9 days	30 days
H. L.	7½	Negative	.....	.....	.....	1 day	16 days
M. B.	4	Negative	.....	.....	.....	15 days	1½ months
G. B.	11	Negative	.....	.....	.....	6 days	17 days
			Positive	.....	.....	6 days	
H. P.	9	Negative	.....	.....	.....	3 days	3½ weeks
E. D.	8	.....	.....	.....	? dose pos.	?	?
I. W.	5	.....	Positive	.....	.....	2 days	13 days
C. W.	11	.....	Pos., 0.01 mg.	.....	.....	4 days	35 days
D. W.	5	.....	Positive	.....	.....	40 days	47 days
E. G.	11	Positive	.....	.....	.....	7 days	8 days
			Positive	.....	.....	7 days	
A. G.	7	.....	Positive	.....	.....	15 days	37 days
O. H.	11¾	.....	Positive	.....	.....	19 days	19 days
R. C.	4	.....	Positive	.....	.....	36 days	40 days
E. J.	7	.....	Positive	.....	.....	41 days	85 days
O. J.	9	.....	Positive	.....	.....	38 days	60 days
L. T.	5	.....	Positive	.....	.....	7 days	23 days
A. T.	7	.....	Positive	.....	.....	21 days	21 days
W. K.	11½	.....	Positive	.....	.....	7 days	31 days
J. M.	7	.....	Positive	.....	.....	1 day	25 days
R. L.	5	.....	Positive	.....	.....	3½ months	4½ months
D. M.	7	.....	Positive	.....	.....	21 days	51 days
T. P.	8	.....	Positive	.....	.....	2 weeks	2½ weeks
K. B.	4	.....	.....	Positive	.....	?	?
F. C.	7	.....	Positive	.....	.....	1 month	3¼ months
E. P.	11	.....	Positive	.....	.....	4 days	3½ weeks
F. P.	5	.....	Positive	.....	.....	3 days	3 days
G. S.	10	.....	Positive	.....	.....	2 weeks	4 weeks
J. S.	10	.....	Positive	.....	.....	?	?
C. B.	11	Positive	.....	.....	.....	2 days	23 days
E. H.	11	Positive	.....	.....	.....	1 day	8 days
A. G.	8	Positive	.....	.....	.....	29 days	41 days
P. G.	7	Positive	.....	.....	.....	?	?
J. D.	3	Positive	.....	.....	.....	7 days	27 days
V. H.	6	Positive	.....	.....	.....	6 days	7½ months
W. L.	2	Positive	.....	.....	.....	8 days	46 days
M. B.	9	Positive	.....	.....	.....	7 days	14 days
L. B.	10	Positive	.....	.....	.....	9 days	11 days
A. C.	9	Positive	.....	.....	.....	4 days	1¼ months
C. S.	5	Positive	.....	.....	.....	?	?
B. M.	5	.. ..	Negative	.....	.....	59 days	77 days
				Positive	.....	65 days	
L. T.	11	. .....	Negative	.....	.....	3 days	6 days
				Positive	.....	3 days	
L. N.	10	. .....	Negative	.....	.....	11 days	44 days
				Positive	.....	8 days	
L. W.	10	. .....	Negative	.....	.....	15 days	26 days
				Positive	.....	11 days	
N. G.	8	. .....	Negative	.....	.....	8 days	13 days
				Positive	.....	6 days	
					Pos., 5 mg.	5 days	
D. D.	4½	. .....	Negative	.....	.....	8 days	13 days
				Positive	.....	9 days	
C. D.	8	.. ..	Negative	.....	.....	?	30 days
				Positive	.....	9 days	
L. J.	8	.. ..	Negative	.....	.....	1 day	25 days
				Positive	.....	3 days	
W. H.	4	.. ..	Negative	.....	.....	16 days	6½ months
				Positive	.....	12 days	
E. W.	11	.....	Negative	.....	.....	4½ months	6¾ months
				Positive	.....	3½ months	

to the skin test. Only three cases showed a negative result when the intradermal dose was increased. Ten cases showed a positive result on having the dose increased.

Roentgen Diagnosis.—Twice as many cases of miliary tuberculosis were missed by the x-rays as were correctly diagnosed. Apparently, tuberculosis of the lungs in infants must be quite far advanced, almost to the point where the tubercles form confluent and caseous masses, before it becomes visible roentgenographically.

DISTRIBUTION OF CASES OCCURRING IN INFANTS UNDER ONE YEAR ACCORDING TO MONTHS

The accompanying chart shows the grouping according to age of infants dying from tuberculosis during the first year. More than twice



Age distribution of cases of tuberculosis in infants under 1 year of age who came to autopsy from 1915 to 1928.

as many children died during the second half of the first year as during the first half.

SUMMARY

Seventy-five cases of tuberculosis in infants under 1 year of age are presented. The pathologic study shows the high incidence of involvement of the tracheobronchial glands, of severe involvement of the lungs with formation of cavities, of intestinal ulceration and of meningitis. The degree of involvement and the rapidity with which it takes place are striking. The Mantoux test is of great diagnostic value in cases of tuberculosis in infants. The x-rays have little practical value in the accurate diagnosis of involvement of the lungs.

PHYSICAL TRAITS OF YOUNG CHILDREN

REPORT OF MEASUREMENTS OF ONE HUNDRED AND FIFTY BOYS AND ONE HUNDRED AND SIXTY-SEVEN GIRLS FROM THREE TO SIX YEARS OF AGE

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Within the last year a number of requests have been received in the Iowa Child Welfare Research Station for averages of physical measurements of young children. In order to meet the demand, tables have been prepared of the means, standard deviations, probable errors and coefficients of variation, in metric units, of the measurements of 150 boys and 167 girls from 3 to 6 years of age who have been enrolled in the preschool psychological laboratories of the station from September, 1922, to April, 1928. These tables are part of a comprehensive study of physical growth, in progress at the station.

The children measured were in good health; the majority belong to the rather favoring social environment provided by parents of the professional and merchant classes.

The measurements, obtained monthly on the date corresponding to the child's birthday, were made by trained workers under the direction of Dr. Bird T. Baldwin; the technic followed is described in his book, "Physical Growth of Children from Birth to Maturity."[1] The children were measured nude, and the measurements recorded in metric units.

For the computation of the mean, standard deviation, probable error of the mean and coefficient of variation for each physical trait, the 512 measurements on the 150 boys and the 568 measurements on the 167 girls were distributed in three-month age groups from 3 to 6 years inclusive. In this grouping a child is considered of a given age if his actual age is within one month and fourteen days less than or one month and fifteen days more than that age; i. e., a child is designated as 3 years and 3 months of age from the age of 3 years, 1 month and 16 days to the age of 3 years, 4 months, and 15 days. Since measurements had been made monthly, the problem arose of selecting one of the three

* Submitted for publication, April 9, 1929.

* Helen V. Garside, statistician in the station, is responsible for the tabulation of the results of the measurements, which were made during the six-year period by Augusta Alpert, Laura Busby, Grace Clark, Gladys F. Davis, Irene Field, Gertrude A. Pavey, Idell Pyle and Beth Wellman.

1. Baldwin, B. T.: The Physical Growth of Children from Birth to Maturity, University of Iowa Studies, Studies in Child Welfare, no. 1, Iowa City, University of Iowa, 1921.

TABLE 1.—*Means, Standard Deviations, Probable Errors and Coefficients of Variation of Sixteen Physical Measurements in Metric Units at Three-Month Intervals of One Hundred and Fifty Boys from 3 to 6 Years of Age*

Physical Measurement	Unit	Boys in Group	Mean	Standard Deviation	Probable Error	Variation	Boys in Group	Mean	Standard Deviation	Probable Error	Variation	Boys in Group	Mean	Standard Deviation	Probable Error	Variation	Boys in Group	Mean	Standard Deviation	Probable Error	Variation
		2 years, 10 months, 16 days to 3 years, 10 months, 15 days																			
		2/10/16 to 3/1/15					3/1/16 to 3/4/15					3/4/16 to 3/7/15					3/7/16 to 3/10/15				
Height: standing	Cm.	23	95.39	3.02	0.42	3.2	37	97.59	3.40	0.38	3.5	35	98.88	3.74	0.43	3.8	32	101.42	3.41	0.41	3.4
sitting	Cm.	23	56.35	1.89	0.27	3.4	37	57.27	1.86	0.21	3.2	34	57.78	1.80	0.21	3.1	32	59.06	1.90	0.23	3.2
Head: anteroposterior diameter	Cm.	23	17.03	0.48	0.07	2.8	37	16.92	0.50	0.06	3.0	35	17.00	0.50	0.06	2.9	32	17.08	0.57	0.07	3.3
transverse diameter	Cm.	23	13.83	0.39	0.05	2.8	37	13.99	0.46	0.05	3.3	35	14.07	0.60	0.07	4.3	32	14.22	0.57	0.07	4.0
circumference	Cm.	23	50.76	0.81	0.11	1.6	37	50.90	1.39	0.15	2.7	35	51.11	1.71	0.19	3.3	32	51.45	1.74	0.21	3.4
Shoulders: width	Cm.	23	23.43	0.90	0.13	3.8	37	23.84	1.08	0.12	4.5	35	23.96	1.21	0.14	5.0	32	24.39	1.15	0.14	4.7
Arms: span	Cm.	17	92.42	3.52	0.58	3.8	29	95.96	3.80	0.48	4.0	26	97.58	4.04	0.53	4.1	28	99.48	3.71	0.47	3.7
shoulder-elbow, left	Cm.	21	19.77	0.85	0.13	4.3	33	20.60	1.00	0.12	4.9	32	20.86	1.06	0.13	5.1	30	21.23	0.95	0.12	4.5
shoulder-elbow, right	Cm.	21	19.82	0.82	0.12	4.1	33	20.58	0.97	0.11	4.7	32	20.86	1.02	0.12	4.9	30	21.27	0.92	0.11	4.3
elbow-finger tip, left	Cm.	21	25.71	0.93	0.14	3.6	33	26.02	1.18	0.14	4.4	33	26.82	1.20	0.14	4.5	30	27.55	1.10	0.14	4.0
elbow-finger tip, right	Cm.	21	25.75	0.91	0.13	3.5	33	26.59	1.20	0.14	4.5	33	26.79	1.21	0.14	4.5	30	27.60	1.08	0.13	3.9
Chest: width	Cm.	23	17.01	0.59	0.08	3.5	37	17.16	0.76	0.08	4.4	35	17.30	0.80	0.09	4.6	32	17.28	0.78	0.09	4.5
depth	Cm.	23	12.60	0.57	0.08	4.5	37	12.74	0.59	0.07	4.6	35	12.92	0.47	0.05	3.6	32	12.98	0.53	0.06	4.1
circumference	Cm.	23	50.92	1.60	0.22	3.1	37	51.70	2.15	0.24	4.2	34	52.26	2.29	0.26	4.4	31	52.49	2.09	0.25	4.0
Hips: width	Cm.	22	17.63	0.73	0.10	4.1	37	18.19	1.00	0.11	5.5	35	18.42	0.86	0.10	4.7	32	18.85	0.82	0.10	4.3
Weight	Kg.	23	14.61	1.00	0.14	6.8	37	15.34	1.42	0.16	9.3	35	16.06	1.74	0.20	10.8	32	16.82	1.82	0.22	10.8
		3 years, 10 months, 16 days to 4 years, 10 months, 15 days																			
		3/10/16 to 4/1/15					4/1/16 to 4/4/15					4/4/16 to 4/7/15					4/7/16 to 4/10/15				
Height: standing	Cm.	32	102.51	3.50	0.42	3.4	38	104.33	3.28	0.36	3.1	47	105.98	3.84	0.38	3.6	39	107.82	3.92	0.42	3.6
sitting	Cm.	32	59.19	1.92	0.23	3.2	38	60.04	1.92	0.21	3.2	47	60.60	2.10	0.21	3.5	39	61.58	2.20	0.24	3.6
Head: anteroposterior diameter	Cm.	32	17.06	0.48	0.06	2.8	38	17.20	0.61	0.07	3.5	47	17.48	0.55	0.05	3.1	39	17.48	0.64	0.07	3.7
transverse diameter	Cm.	32	14.29	0.48	0.06	3.4	37	14.32	0.60	0.07	4.2	47	14.37	0.60	0.06	4.2	38	14.27	0.60	0.07	4.2
circumference	Cm.	32	51.32	1.12	0.13	2.2	38	51.64	1.43	0.16	2.8	47	52.18	1.29	0.13	2.5	39	52.00	1.70	0.18	3.3
Shoulders: width	Cm.	32	24.57	0.98	0.12	4.0	38	24.92	1.08	0.12	4.3	46	25.12	1.17	0.12	4.7	39	25.45	1.18	0.13	4.6
Arms: span	Cm.	27	100.64	4.44	0.58	4.4	31	102.97	3.82	0.46	3.7	43	104.53	4.10	0.42	3.9	37	106.30	4.53	0.50	4.3
shoulder-elbow, left	Cm.	29	21.56	1.18	0.15	5.5	36	22.00	0.92	0.10	4.2	47	22.25	1.05	0.10	4.7	39	22.50	0.98	0.11	4.4
shoulder-elbow, right	Cm.	29	21.63	1.14	0.14	5.3	36	22.06	0.94	0.11	4.3	47	22.26	1.04	0.10	4.7	39	22.54	0.96	0.11	4.3
elbow-finger tip, left	Cm.	29	27.76	1.18	0.15	4.2	36	28.32	1.17	0.13	4.1	45	28.78	1.22	0.12	4.2	39	29.20	1.15	0.13	3.9
elbow-finger tip, right	Cm.	29	27.79	1.15	0.14	4.1	36	28.29	1.10	0.12	3.9	46	28.74	1.20	0.12	4.2	39	29.21	1.19	0.13	4.1
Chest: width	Cm.	32	17.46	0.64	0.08	3.7	38	17.64	0.84	0.09	4.8	47	17.87	0.75	0.07	4.2	39	17.85	0.96	0.11	5.4
depth	Cm.	32	13.26	0.55	0.07	4.1	38	13.29	0.57	0.06	4.3	47	13.26	0.72	0.07	5.4	39	13.28	0.69	0.07	5.2
circumference	Cm.	32	52.81	1.98	0.24	3.7	36	53.18	1.80	0.20	3.4	46	53.63	1.74	0.17	3.2	39	53.63	2.06	0.22	3.8
Hips: width	Cm.	32	19.00	0.92	0.11	4.8	38	19.09	0.85	0.09	4.5	47	19.26	0.92	0.09	4.8	39	19.41	0.82	0.09	4.2
Weight	Kg.	32	17.01	1.64	0.20	9.6	38	17.42	1.66	0.18	9.5	47	17.90	1.63	0.16	9.1	39	18.10	1.99	0.21	11.0

		4 years, 10 months, 16 days to 5 years, 10 months, 15 days																			
		4/10/16 to 5/1/15					5/1/16 to 5/4/15					5/4/16 to 5/7/15					5/7/16 to 5/10/15				
Height: standing	Cm.	50	109.32	3.61	0.34	3.3	53	111.08	4.45	0.41	4.0	54	112.68	4.13	0.38	3.7	36	114.58	4.43	0.50	3.9
sitting	Cm.	50	62.05	2.25	0.21	3.6	53	62.80	2.72	0.25	4.3	54	63.60	2.46	0.23	3.9	36	64.03	2.78	0.31	4.3
Head: anteroposterior diameter	Cm.	50	17.55	0.75	0.07	4.3	53	17.74	0.69	0.06	3.9	54	17.71	0.62	0.06	3.5	36	17.62	0.74	0.08	4.2
transverse diameter	Cm.	50	14.31	0.52	0.05	3.6	53	14.35	0.56	0.05	3.9	53	14.42	0.55	0.05	3.8	36	14.41	0.59	0.07	4.1
circumference	Cm.	50	52.11	1.60	0.15	3.1	53	52.52	1.60	0.15	3.0	54	52.43	1.25	0.11	2.4	36	52.45	1.60	0.18	3.0
Shoulders: width	Cm.	50	25.47	1.02	0.10	4.0	53	25.98	1.14	0.11	4.4	54	26.22	1.13	0.10	4.3	36	26.39	1.24	0.14	4.7
Arms: span	Cm.	48	107.13	3.81	0.37	3.6	50	109.10	4.44	0.42	4.1	53	110.53	4.04	0.37	3.7	33	112.04	4.16	0.49	3.7
shoulder-elbow, left	Cm.	50	22.78	0.99	0.09	4.3	53	23.28	1.02	0.09	4.4	54	23.61	1.14	0.10	4.8	36	23.79	0.96	0.11	4.0
shoulder-elbow, right	Cm.	50	22.83	0.98	0.09	4.3	53	23.33	1.00	0.09	4.3	54	23.64	1.11	0.10	4.7	36	23.83	0.94	0.11	3.9
elbow-finger tip, left	Cm.	50	29.50	1.03	0.10	3.5	53	30.11	1.35	0.13	4.5	54	30.31	1.17	0.11	3.9	36	30.09	1.15	0.13	3.7
elbow-finger tip, right	Cm.	50	29.53	1.06	0.10	3.6	53	30.13	1.35	0.13	4.5	54	30.36	1.19	0.11	3.9	36	30.76	1.21	0.14	3.9
Chest: width	Cm.	50	17.76	0.73	0.07	4.1	53	18.24	0.89	0.08	4.9	54	18.37	0.79	0.07	4.3	36	18.39	0.98	0.11	5.3
depth	Cm.	50	13.39	0.65	0.06	4.9	53	13.50	0.68	0.06	5.0	54	13.73	0.85	0.08	6.2	36	13.70	0.78	0.09	5.7
circumference	Cm.	47	54.12	1.78	0.18	3.3	53	54.82	1.96	0.18	3.6	54	55.37	1.90	0.17	3.4	36	55.43	2.32	0.26	4.2
Hips: width	Cm.	50	19.59	0.85	0.08	4.3	53	19.81	0.90	0.09	4.8	54	20.00	1.04	0.10	5.2	36	20.11	1.04	0.12	5.2
Weight	Kg.	50	18.69	1.90	0.18	10.2	53	19.20	2.07	0.19	10.8	54	19.83	1.92	0.18	9.7	36	19.92	2.19	0.25	11.0

		5 years, 10 months, 16 days to 6 years, 1 month, 15 days				
		5/10/16 to 6/1/15				
Height: standing	Cm.	36	115.32	4.17	0.47	3.6
sitting	Cm.	36	64.04	2.38	0.27	3.7
Head: anteroposterior diameter	Cm.	36	17.57	0.65	0.07	3.7
transverse diameter	Cm.	36	14.34	0.58	0.07	4.0
circumference	Cm.	36	52.27	1.44	0.16	2.8
Shoulders: width	Cm.	36	26.34	0.99	0.11	3.8
Arms: span	Cm.	36	112.90	3.81	0.43	3.4
shoulder-elbow, left	Cm.	36	24.04	1.04	0.12	4.3
shoulder-elbow, right	Cm.	36	24.11	1.04	0.12	4.3
elbow-finger tip, left	Cm.	36	30.85	1.15	0.13	3.7
elbow-finger tip, right	Cm.	36	30.89	1.12	0.13	3.6
Chest: width	Cm.	36	18.36	0.91	0.10	5.0
depth	Cm.	36	13.87	0.75	0.08	5.4
circumference	Cm.	36	55.86	2.16	0.24	3.9
Hips: width	Cm.	36	20.20	0.92	0.10	4.6
Weight	Kg.	36	20.29	2.41	0.27	11.9

TABLE 2.—*Means, Standard Deviations, Probable Errors and Coefficients of Variation of Sixteen Physical Measurements in Metric Units at Three-Month Intervals of One Hundred and Sixty-Seven Girls from 3 to 6 Years of Age*

Physical Measurement	Unit	Girls in Group	Mean	Standard Deviation	Probable Error	Variation	Girls in Group	Mean	Standard Deviation	Probable Error	Variation	Girls in Group	Mean	Standard Deviation	Probable Error	Variation	Girls in Group	Mean	Standard Deviation	Probable Error	Variation
		2 years, 10 months, 16 days to 3 years, 10 months, 15 days																			
		2/10/16 to 3/1/15					3/1/16 to 3/4/15					3/4/16 to 3/7/15					3/7/16 to 3/10/15				
Height: standing	Cm.	38	95.28	2.56	0.28	2.7	47	96.58	3.13	0.31	3.2	38	97.78	3.71	0.41	3.8	43	100.87	3.72	0.38	3.7
sitting	Cm.	37	55.88	1.54	0.17	2.8	47	56.36	2.06	0.20	3.7	38	56.91	2.37	0.26	4.2	43	58.10	2.00	0.21	3.4
Head: anteroposterior diameter	Cm.	37	16.62	0.49	0.05	2.9	47	16.58	0.47	0.05	2.8	38	16.53	0.62	0.07	3.7	42	16.73	0.58	0.06	3.5
transverse diameter	Cm.	37	13.52	0.48	0.05	3.5	47	13.58	0.44	0.04	3.2	38	13.61	0.36	0.04	2.6	42	13.59	0.50	0.05	3.7
circumference	Cm.	38	49.06	0.98	0.11	2.0	46	49.71	1.19	0.12	2.4	37	49.69	1.16	0.13	2.3	43	49.90	1.26	0.13	2.5
Shoulders: width	Cm.	38	23.51	0.86	0.09	3.7	47	23.51	1.03	0.10	4.4	38	23.69	0.86	0.09	3.6	43	23.91	1.07	0.11	4.5
Arms: span	Cm.	28	92.85	2.51	0.32	2.7	36	93.98	3.53	0.40	3.8	30	95.16	3.95	0.49	4.1	35	97.43	3.94	0.45	4.0
shoulder-elbow, left	Cm.	31	19.84	0.76	0.09	3.8	44	20.03	1.11	0.11	5.5	35	20.26	1.07	0.12	5.3	41	20.60	1.11	0.12	5.4
shoulder-elbow, right	Cm.	31	19.83	0.73	0.09	3.7	44	20.03	1.09	0.11	5.4	35	20.29	1.05	0.12	5.2	41	20.61	1.08	0.11	5.2
elbow-finger tip, left	Cm.	31	25.65	0.78	0.09	3.0	44	25.72	1.07	0.11	4.2	35	26.06	1.01	0.12	3.9	41	26.09	0.97	0.10	3.6
elbow-finger tip, right	Cm.	31	25.61	0.75	0.09	2.9	44	25.73	1.06	0.11	4.1	35	26.08	1.00	0.11	3.8	41	26.73	0.98	0.10	3.7
Chest: width	Cm.	38	16.68	0.69	0.08	4.1	47	16.68	0.77	0.08	4.6	38	16.64	0.76	0.08	4.6	43	16.86	0.87	0.09	5.2
depth	Cm.	38	12.40	0.63	0.07	5.1	47	12.36	0.64	0.06	5.2	38	12.39	0.65	0.07	5.2	43	12.43	0.69	0.07	5.6
circumference	Cm.	38	50.55	1.69	0.18	3.3	46	50.36	2.08	0.21	4.1	38	50.33	2.21	0.24	4.4	43	50.71	2.34	0.24	4.6
Hips: width	Cm.	38	18.16	0.80	0.09	4.4	47	18.29	0.94	0.09	5.1	38	18.30	1.05	0.11	5.7	43	18.58	0.92	0.09	5.0
Weight	Kg.	37	14.75	1.19	0.13	8.1	47	14.93	1.48	0.15	9.9	38	14.97	1.53	0.17	10.2	43	15.72	1.70	0.17	11.3
		3 years, 10 months, 16 days to 4 years, 10 months, 15 days																			
		3/10/16 to 4/1/15					4/1/16 to 4/4/15					4/4/16 to 4/7/15					4/7/16 to 4/10/15				
Height: standing	Cm.	42	101.40	4.20	0.44	4.1	47	103.10	4.10	0.40	4.0	49	105.31	3.97	0.38	3.8	48	107.23	3.05	0.30	2.8
sitting	Cm.	41	58.41	2.47	0.26	4.2	47	59.28	2.18	0.21	3.7	49	60.20	2.18	0.21	3.6	48	60.87	1.74	0.17	2.9
Head: anteroposterior diameter	Cm.	40	16.76	0.61	0.07	3.6	46	16.81	0.54	0.05	3.2	49	16.78	0.54	0.05	3.2	48	16.78	0.52	0.05	3.1
transverse diameter	Cm.	41	13.61	0.54	0.06	4.0	46	13.67	0.48	0.05	3.5	49	13.75	0.43	0.04	3.1	48	13.77	0.43	0.04	3.1
circumference	Cm.	41	49.88	1.40	0.15	2.8	47	50.13	1.32	0.13	2.6	49	50.11	1.20	0.12	2.4	48	50.20	1.18	0.11	2.4
Shoulders: width	Cm.	42	23.97	0.98	0.10	4.1	47	24.24	0.98	0.10	4.0	48	24.68	1.06	0.10	4.3	48	24.94	1.23	0.12	4.9
Arms: span	Cm.	32	98.15	4.58	0.55	4.7	41	99.89	4.52	0.48	4.5	43	102.49	3.34	0.34	3.3	45	103.97	3.27	0.33	3.1
shoulder-elbow, left	Cm.	40	20.85	0.99	0.11	4.7	45	21.07	1.14	0.11	5.4	46	21.59	1.02	0.10	4.7	48	22.19	1.09	0.11	4.9
shoulder-elbow, right	Cm.	40	20.92	0.99	0.11	4.7	45	21.10	1.16	0.12	5.5	46	21.66	0.96	0.10	4.4	48	22.24	1.08	0.11	4.9
elbow-finger tip, left	Cm.	40	27.04	1.08	0.12	4.0	45	27.33	1.04	0.10	3.8	46	27.85	1.06	0.11	3.8	48	28.33	0.96	0.09	3.4
elbow-finger tip, right	Cm.	40	27.03	1.12	0.12	4.1	45	27.38	1.07	0.11	3.9	46	27.86	1.01	0.10	3.6	48	28.31	0.94	0.09	3.3
Chest: width	Cm.	42	16.80	0.87	0.09	5.2	47	16.97	0.84	0.08	4.9	48	17.29	0.78	0.08	4.5	48	17.40	0.94	0.09	5.4
depth	Cm.	42	12.51	0.56	0.06	4.5	47	12.62	0.64	0.06	5.1	48	12.71	0.61	0.06	4.8	48	12.79	0.73	0.07	5.7
circumference	Cm.	40	50.68	2.15	0.23	4.2	47	51.29	2.26	0.22	4.4	49	51.68	2.03	0.20	3.9	48	52.31	2.64	0.26	5.0
Hips: width	Cm.	42	18.57	0.98	0.10	5.3	47	18.79	1.06	0.10	5.6	48	19.14	0.98	0.10	5.1	47	19.46	0.91	0.09	4.7
Weight	Kg.	42	15.78	1.64	0.17	10.4	47	16.51	1.93	0.19	11.7	49	17.18	1.71	0.16	10.0	48	17.61	1.77	0.17	10.1

		4 years, 10 months, 16 days to 5 years, 10 months, 15 days																			
		4/10/16 to 5/1/15					5/1/16 to 5/4/15					5/4/16 to 5/7/15					5/7/16 to 5/10/15				
Height: standing	Cm.	52	109.02	3.80	0.36	3.5	47	110.47	3.29	0.32	3.0	47	111.98	3.86	0.38	3.4	39	113.18	3.95	0.43	3.5
sitting	Cm.	52	61.69	2.08	0.19	3.4	47	62.30	2.10	0.21	3.4	47	62.81	2.08	0.20	3.3	39	63.20	2.28	0.25	3.6
Head: anteroposterior diameter	Cm.	52	16.89	0.45	0.04	2.7	47	16.95	0.50	0.05	2.9	47	17.04	0.49	0.05	2.9	39	17.09	0.53	0.06	3.1
transverse diameter	Cm.	52	13.76	0.41	0.04	3.0	47	13.77	0.47	0.05	3.4	47	13.74	0.44	0.04	3.2	39	13.77	0.48	0.05	3.5
circumference	Cm.	52	50.39	1.14	0.11	2.3	47	50.59	1.33	0.13	2.6	47	50.34	1.17	0.12	2.3	39	50.37	1.04	0.11	2.1
Shoulders: width	Cm.	52	25.10	1.25	0.12	5.0	47	25.50	1.42	0.14	5.6	47	25.66	1.40	0.14	5.5	39	25.87	1.32	0.14	5.1
Arms: span	Cm.	47	105.20	3.77	0.37	3.6	45	107.41	3.73	0.37	3.5	45	108.33	4.00	0.40	3.7	36	109.81	4.69	0.53	4.3
shoulder-elbow, left	Cm.	52	22.49	1.10	0.10	4.9	47	22.93	0.92	0.09	4.0	47	23.20	0.97	0.10	4.2	39	23.30	1.07	0.12	4.6
shoulder-elbow, right	Cm.	52	22.55	1.04	0.10	4.6	47	22.97	0.88	0.09	3.8	47	23.22	0.96	0.09	4.1	39	23.34	1.04	0.11	4.5
elbow-finger tip, left	Cm.	52	28.69	1.04	0.10	3.6	47	29.18	1.04	0.10	3.6	47	29.50	1.09	0.11	3.7	39	29.91	1.25	0.14	4.2
elbow-finger tip, right	Cm.	52	28.67	1.08	0.10	3.8	47	29.23	1.00	0.10	3.4	47	29.56	1.13	0.11	3.8	39	29.93	1.26	0.14	4.2
Chest: width	Cm.	52	17.43	1.22	0.11	7.0	47	17.71	1.14	0.11	6.4	47	17.65	0.96	0.09	5.4	39	17.79	0.99	0.11	5.6
depth	Cm.	52	12.99	0.88	0.08	6.8	47	13.14	0.73	0.07	5.6	47	13.17	0.73	0.07	5.5	39	13.24	0.77	0.08	5.8
circumference	Cm.	52	52.42	2.58	0.24	4.9	47	53.09	2.57	0.25	4.8	47	53.12	2.56	0.25	4.8	39	53.76	2.34	0.25	4.4
Hips: width	Cm.	52	19.73	0.87	0.08	4.4	47	19.90	1.05	0.10	5.3	47	19.84	1.01	0.10	5.1	39	20.09	1.11	0.12	5.5
Weight	Kg.	52	17.95	1.88	0.18	10.5	46	18.39	2.28	0.23	12.4	47	18.51	2.27	0.22	12.3	39	19.29	2.51	0.27	13.0

		5 years, 10 months, 16 days to 6 years, 1 month, 15 days				
		5/10/16 to 6/1/15				
Height: standing	Cm.	31	114.44	4.16	0.50	3.6
sitting	Cm.	31	63.78	2.25	0.27	3.5
Head: anteroposterior diameter	Cm.	30	17.14	0.57	0.07	3.3
transverse diameter	Cm.	31	13.87	0.54	0.07	3.9
circumference	Cm.	31	50.44	0.97	0.12	1.9
Shoulders: width	Cm.	31	26.06	1.20	0.15	4.6
Arms: span	Cm.	30	110.74	4.44	0.55	4.0
shoulder-elbow, left	Cm.	31	23.57	1.10	0.13	4.7
shoulder-elbow, right	Cm.	31	23.64	1.11	0.13	4.7
elbow-finger tip, left	Cm.	31	30.05	1.28	0.16	4.3
elbow-finger tip, right	Cm.	31	30.09	1.30	0.16	4.3
Chest: width	Cm.	31	17.94	0.96	0.12	5.4
depth	Cm.	31	13.31	0.83	0.10	6.2
circumference	Cm.	31	54.02	2.28	0.28	4.2
Hips: width	Cm.	31	20.44	1.30	0.16	6.4
Weight	Kg.	31	19.60	2.57	0.31	13.1

sets of measurements for a particular three-month group, since each child was used only once in a given group. If the three available sets had equally complete data, the set of measurements nearest the middle, that is, the class mark, of the interval was used; otherwise, the set having the fullest data on all desired physical traits was used. This method was followed because it tended to make the cases pile up at the class mark; this is more desirable than having them concentrated at either extreme.

THE POLYMORPHONUCLEAR COUNT IN THE NEW-BORN

II. DEFLECTION BY THE ULTRAVIOLET LIGHT*

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During the study of the action of the ultraviolet light on the blood of the new-born infant, it was found that there was an increase in the white blood cells and a change in their morphology.[1] It was therefore considered desirable to study this action in detail.

METHOD

This study is based on a series of 100 new-born infants, during a period of ten months. The differential counts were made within six hours after birth and at twenty-four hour intervals thereafter. The determinations were made at the same time every day. The slides were stained with carbol-pyronin,[2] the films being dried in air and the stain applied for fifteen minutes. No preliminary fixation is required after washing and drying. The slides are examined unmounted. The stain imparts a deep blue color to the nuclei and a pink color to the cytoplasm. The red cells stain feebly pink.

In drawing the blood to make the determinations, the skin of the heel was thoroughly cleansed with green soap and water, and finally with alcohol. A deep puncture was then made in the heel, which resulted in an adequate flow of blood. To insure a free flow, three drops were allowed to fall as a routine.

The treatments with the ultraviolet ray were given by means of an air cooled mercury vapor quartz lamp of 110 volts, 60 cycles, and 10 amperes. A voltage of 70 was always administered and maintained throughout the exposures. Treatments were begun on the second day of life. The dorsal and ventral surfaces were first exposed for one minute each, and the time was increased one minute a day until the fourth day.

Cooke's classification, which he has termed "the polynuclear count," was used. The polymorphonuclear leukocyte with an individual nucleus is placed in class I; the cell in which the nucleus has divided into two lobes is placed in class II; the cell with three lobes in class III, and the cell with four lobes in class IV. Nuclei without a cell body or those subjected to pressure were not counted. One hundred cells were counted in each slide. So that the changes in the various classes might be appreciated better, the weighted mean, devised by Cooke and Ponder, was used. This is obtained by multiplying the number of cells in class I by one, those in class II by two, in class III by three, and in class IV by four. The results are added and divided by the total number of cells.

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* Submitted for publication, April 13, 1929.

* From the Department of Pediatrics, Rush Medical College of the University of Chicago, and the Presbyterian Hospital.

1. Sanford, Heyworth N.: The Effect of Ultraviolet Light on the Blood of New-Born Infants: III. The White Cells, Am. J. Dis. Child. **37**:1187 (June) 1929.

2. Cooke, W. E., and Ponder, Eric: The Polynuclear Count, Philadelphia, J. B. Lippincott Company, 1927.

The results of the experiment are shown in the following table:

Results of Tests

Day	Class I	Class II	Class III	Class IV	Mean
1	57	38	5	..	1.48
2	62	35	3	..	1.41
3	40	27	29	4	2.07
4	74	22	4	..	1.30
5	71	25	4	..	1.33
6	71	29	..	..	1.29
7	78	22	..	..	1.22
8	68	32	..	..	1.32
9	53	38	9	..	1.56
10	50	33	17	..	1.67

COMMENT

In the normal new-born, the polymorphonuclears show a considerable variation from those of the adult.[3] On the first day the cells of class I predominate, and the sum of class I and class II is 97 cells. The number of cells of class I falls rapidly to 33 by the tenth day, and that of class II falls slowly, so that they are more numerous than those of class I. The total sum of class I and class II cells is now 67 cells. The cells of class III increase rapidly from the first day, and cells of class IV appear on the ninth day. As no increase is seen in the cells of class I, but rather a sharp decrease, and as the total leukocyte count is not increasing but decreasing, the cells of class III and class IV and in part of class II must be derived from class I.

In the series of new-born infants exposed to ultraviolet irradiation, the effect was seen on the third day. The cells of class I and class II were sharply decreased, while the cells of class III showed an immense increase. Class IV showed 4 cells, which did not normally appear until the ninth day. The following day there was an immense left-handed shift; the cells of class I had almost doubled, while class III cells had decreased to 4. This was more marked on the sixth day of life or the last day of irradiation, when the cells of class III had entirely disappeared. Class I cells increased to their maximum on the day following the final ultraviolet exposure, and then slowly fell toward their normal value by the tenth day.

This is best shown by the weighted mean. On the day following ultraviolet irradiation, the mean had rapidly risen to 2.07. The following day, the preponderance of young cells had forced the mean down to 1.30. Continued ultraviolet exposure drove the mean lower until the minimum of 1.22 was reached on the seventh day. With the cessation of ultraviolet exposures the mean gradually returned toward

3. Sanford, Heyworth N.: The Polynuclear Count in the New-Born: I. Preliminary Study, Am. J. Dis. Child. **38**:271 (Aug.) 1929.

the normal value as the system adjusted itself, reaching 1.67 on the tenth day.

The polymorphonuclear population of the blood vessels is only a fraction of the whole population of circulating polymorphonuclears in the body. These cells abound in the extravascular spaces from which they are continually entering the blood stream and into which they are continually passing from the vessels. The young cells of class I, and occasionally class II, are the only ones that are formed in the hematopoietic system. These later mature in the blood stream to the older cells of classes II, III, and IV. In the normal new-born child, the life cycle of the polymorphonuclear has only just begun, hence the slow growth to classes II, III and IV. The effect of ultraviolet irradiation on this system is apparently to destroy the normal balance by stimulating the hematopoietic system to the excess formation of young cells of class I, and to remove the older cells of class III. Immediately after the first irradiation on the third day, one finds a few cells of class IV that do not appear normally until the ninth day. This is followed by a loss of older cells of class III. The system probably attempts to keep in balance by adding new cells of class I, which is not so apparent as real, because the total leukocytes are decreasing normally in the new-born system.

A similar unbalancing of the normal system has been effected by Ponder [4] by the injecting of thyroid extract into rabbits. Colchicine, nucleic acid and trypsin also cause a polymorphonuclear leukocytosis and a similar deflection of the normal count.

Kennedy and Grover [5] have obtained similar results with single roentgen exposures, and Kennedy and Thompson [6] obtained a removal of the higher classes of leukocytes with a compensatory increase in young cells of class I by exposing rabbits to ultraviolet light.

It has been assumed that the principal blood-forming area was the bone-marrow. When thyroid extract or any of the hematopoietic stimulants is injected into the blood stream, the increase in young cells of class I could be effected by stimulation of the bone marrow. The bone marrow could also be influenced by the roentgen rays. The absorption of ultraviolet light from the skin is great, but penetration of the tissues is possible for only a short distance, so that the bone

4. Ponder, Eric: Studies on Arneth Count: Deflection of Count by Thyroid Injections, Quart. J. Exper. Physiol. **16**:227 (Aug.) 1926.

5. Kennedy, W. P., and Grover, C. A.: Studies on the Arneth Count: Deflection of the Count by the X-Ray, Quart. J. Exper. Physiol. **18**:79 (July) 1927.

6. Kennedy, W. P., and Thompson, W. A. R.: Studies on the Arneth Count: Deflection of the Count by Ultraviolet Rays, Quart. J. Exper. Physiol. **18**:263 (Dec.) 1927.

marrow could not be greatly influenced. This would point more to a stimulation of the hematopoietic system to replace older forms destroyed than to a mere formation of new cells.

SUMMARY

Short exposures to the ultraviolet light tend to increase the number of young or single-lobed nucleated cells of the polymorphonuclears. The older or multilobed forms are decreased. There is a rapid return to normal.

820 North Michigan Avenue.

Case Reports

PAROXYSMAL TACHYCARDIA WITH SYNCOPE OCCURRING IN A CHILD*

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The occurrence of paroxysmal tachycardia in infancy and in childhood is extremely rare, and few authentic cases have been recorded in medical literature. The youngest patient in a reported case was an infant, aged 4 days, whose case was reported by Werley.[1] The type of tachycardia was not identified because electrocardiograms were not taken, but polygraphic tracings showed the rate of the heart to be 307 a minute. Necropsy revealed a widely patent foramen ovale; distinctive microscopic changes were not evident.

Colgate and McCulloch[2] reported two cases of paroxysmal tachycardia in infancy; one occurred in a child, aged 21 days, and the other in a child, aged 24 days. In the first case the rate of the heart was 250 during a paroxysm, but since electrocardiograms were not obtained, the type of tachycardia was not determined. In the second case, electrocardiograms revealed changes that the authors concluded were paroxysms of auricular tachycardia; the rate was 291. The children in both cases recovered.

A case of paroxysmal auricular flutter with a 1:1 rhythm was observed by Lewis[3] in an infant aged 3 months. The rate varied from 270 to 290 a minute. The course of the disease was not reported. A case of auricular flutter with 2:1 rhythm, and paroxysms in which the rate was 1:1, was seen by Poynton and Wyllie[4] in a male infant aged 4 months. The heart was enlarged, but the cause of the car-

* Submitted for publication April 18, 1929.

* From the Sections on Cardiology and Pediatrics, the Mayo Clinic.

1. Werley, G.: Paroxysmal Tachycardia, with Ventricular Rate of 307, in a Child Four Days Old, Arch. Pediat. **62**:825, 1925.

2. Colgate, C. E., and McCulloch, Hugh: Paroxysmal Tachycardia in Infancy; Report of Two Cases with Comments on the Differential Diagnosis, Am. Heart J. **2**:160, 1926.

3. Lewis, Thomas: Lectures on the Heart, New York, Paul B. Hoeber, 1915, p. 116.

4. Poynton, F. J., and Wyllie, W. G.: Auricular Flutter in Infancy, Lancet **2**:371, 1926.

diopathy was unknown. O'Flyn [5] observed paroxysmal tachycardia in an infant, aged 8 months. Rates of 200 and 300 were recorded, but electrocardiograms were not obtained.

Examples of paroxysmal tachycardia in older children have been reported by several observers. Koplik [6] reported three cases which are of interest. The first patient, a child aged 20 months, displayed attacks of paroxysmal cardiac acceleration, ranging from 224 to 280 a minute. The electrocardiograms revealed auricular tachycardia. Koplik concluded that the basis of the tachycardia was infectious myocarditis resulting from influenza. In the second case, which occurred in a child aged 3 years, electrocardiograms revealed alterations which Koplik concluded indicated that the disorder was of supraventricular origin. Analysis of these curves clearly identifies nodal (A-V) tachycardia. The rate was 250 a minute. There was no demonstrable evidence of cardiac disease. In the third case paroxysms of tachycardia, which proved to be flutter and auricular tachycardia, occurred in a child aged 10 years. The ventricular rates ranged from 180 to 225 beats a minute. Information regarding the subsequent course of these patients is not recorded.

A case of paroxysmal tachycardia in a child, aged 2 years, was reported by Hoffmann,[7] and Dressler and Löwy [8] observed a boy aged 2½ years with paroxysmal auricular flutter. Hutchinson and Parkinson [9] reported the case of a child, aged 2 years and eight months, in whom the cardiac rate attained 245 a minute. Electrocardiograms were obtained, but the type of tachycardia was not specified. The child was known to be alive and in good health ten years later. One or two short attacks of tachycardia occurred yearly. Kidd [10] observed paroxysmal tachycardia of unknown type in a child aged 4½ years. A case of paroxysmal tachycardia in childhood was also recorded by Thompson.[11] A case of auricular flutter occurring in a child aged 4½ years with congenital heart disease was reported by us.[12] Varying degrees of block in ratios of from 2:1 to 4:1 occurred. The child was

5. O'Flyn, J. L.: Paroxysmal Tachycardia in an Infant, Brit. M. J. **1**:507, 1925.

6. Koplik, Henry: Paroxysmal Tachycardia in Children, Am. J. M. Sc. **154**: 834, 1917.

7. Hoffmann, quoted by von Bernuth: Ztschr. f. Kinderh. **47**:94, 1929.

8. Dressler, Wilhelm, and Löwy, Moritz: Ueber paroxysmale Tachykardie im Kindesalter, Med. Klin. **22**:1481, 1926.

9. Hutchinson, R., and Parkinson, J.: Paroxysmal Tachycardia in a Child, Brit. M. J. **1**:534, 1914.

10. Kidd, Percy, quoted by Hutchinson and Parkinson (footnote 9).

11. Thompson, J., quoted by Colgate and McCulloch (footnote 2).

12. Amberg, Samuel, and Willius, F. A.: Auricular Flutter with Congenital Heart Disease, Am. J. Dis. Child **32**:99 (July) 1926.

under observation for two years and finally died from congestive cardiac failure. Necropsy revealed a widely open foramen ovale with enormous hypertrophy of the right auricle.

Dressler and Löwy interpreted the electrocardiogram which Sachs obtained in the case of a child aged 3 years also as representative of paroxysmal auricular flutter, whereas Sachs [13] himself regarded it as representative of nodal rhythm. In this case the heart was enlarged, and the child died a year later. The ventricular rate was 240 beats a minute. In the case of a boy, aged 8 years, Cassidy [14] observed auricular tachycardia without evidence of organic involvement of the heart.

Franke and Wiener [15] published electrocardiograms of a boy aged 10 years and of a girl aged 11 years. The former represented a case of nodal tachycardia without other cardiac manifestations in the probable presence of congenital syphilis. In the second case there was a suggestion of mitral endocarditis; the rate of the heart was 240. Franke and Wiener suggested that the cause in these cases was ventricular tachycardia, but the published curve indicates clearly auricular flutter with a 2:1 rhythm. The rate was 250. In this case embolism of both popliteal arteries necessitated amputation of the legs later.

A number of other observations are less clear and therefore are mentioned only briefly. Here belongs a case of paroxysmal tachycardia in the course of chorea in a girl, aged 9 years, and the case of a girl, aged 12 years, in whom the left phrenic nerve was destroyed on account of bronchiectasis. In this case the attacks occurred when the child lay down after a meal. Another case was that of a boy, aged 15 years, with progressive muscular dystrophy. These three cases were reported by von Bernuth;[16] the last case was also reported by Schliephake.[17]

The brief report of Faerber [18] includes the case of a girl aged 4 years with a decompensated heart and that of a boy aged 13 years with a congenital lesion of the heart.

Schuster and Paterson [19] described the heart of an infant aged 8½ weeks in whom paroxysms of tachycardia at a rate of 200 a minute had

13. Sachs, H.: Zur paroxysmalen Tachykardie, Zentralbl. f. Hers- u. Gefässkr. **17**:65, 1926.

14. Cassidy, M. A.: Case of Incessant Paroxysmal Tachycardia in a Child, Proc. Roy. Soc. Med. **18**:14, 1925.

15. Franke, Wolfgang, and Wiener, Rudolf: Die paroxysmale Tachykardie im Kindesalter, Ztschr. f. Kinderh. **46**:676, 1928.

16. Von Bernuth, Fritz: Ueber paroxysmale Tachykardie im Kindesalter, Ztschr. f. Kinderh. **47**:94, 1929.

17. Schliephake, Erwin: Der kardio-intestinale Symptomenkomplex bei der progressiven Muskeldystrophie, Ztschr. f. Kinderh. **47**:85, 1929.

18. Faerber: Paroxysmal Tachykardie, Klin. Wchnschr. **5**:202, 1926.

19. Schuster, Norah H., and Paterson, Donald: Specimen from a Case of Paroxysmal Tachycardia in an Infant, Aged Nine Weeks, Proc. Roy. Soc. Med. **17**:11, 1924.

occurred. Unusual congenital anomalies existed. The left ventricle was hypertrophied and dilated. The pulmonary artery arose from the left ventricle, whereas the aorta came from the right ventricle. The ductus arteriosus was widely patent.

A summary of the previously reported cases and of the case comprising this report is given in the accompanying table.

Summary of the Reported Cases of Paroxysmal Cardiac Acceleration in Children

Case	Author	Age	Type of Paroxysmal Cardiac Acceleration	Cardiac Rate, Beats Each Minute: Ventricular	Cardiac Rate, Beats Each Minute: Auricular	Type of Cardiac Disease
1	Colgate and McCulloch.	24 days	Auricular tachycardia	291	...	None
2	Koplik.....	20 months	Auricular tachycardia	224–280	...	Infectious myocarditis
3	Cassidy.....	8 years	Auricular tachycardia	?	...	None
4	Poynton and Wyllie.....	4 months	Auricular flutter.....	? ?	...	Cardiac hypertrophy
5	Dressler and Löwy.....	2.5 years	Auricular flutter.....	260	...	?
6	Koplik.....	10 years	Auricular flutter.....	180–225	...	?
7	Lewis.....	3 months	Auricular flutter.....	270–290	...	?
8	Amberg and Willius.....	4.5 years	Auricular flutter.....	71–105	315 330	Patent foramen ovale with great hypertrophy of the right auricle
9	Franke and Wiener.....	11 years	Auricular flutter.....	240	500	Questionable endocarditis
10	Willius and Amberg....	7 years	Nodal tachycardia....	156	...	Focal myocarditis (?)
11	Koplik.....	3 years	Nodal tachycardia....	250	...	None
12	Franke and Wiener.....	10 years	Nodal tachycardia....	240–250	...	Congenital syphilis
13	Colgate and McCulloch.	21 days	Not identified.....	250	...	None
14	O'Flyn.....	8 months	Not identified.....	200–300	...	?
15	Hutchinson and Parkinson.....	2.75 years	Not identified.....	245	...	?
16	Kidd.....	4.5 years	Not identified.....	?	...	?
17	Thompson...	2 years	Not identified.....	?	...	?
18	Werley.....	4 days	Not identified.....	307	...	?
19	von Bernuth	9 years	Not identified.....	180	...	?
20	von Bernuth	12 years	Not identified.....	180–200	...	?
21	von Bernuth	15 years	Not identified.....	160	...	?
22	Schuster and Paterson..	8.5 weeks	Not identified.....	200	...	Congenital cardiac disease
23	Faerber.....	4 years	Not identified.....	?	...	Cardiac failure
24	Faerber.....	13 years	Not identified.....	?	...	Congenital lesion of the heart

REPORT OF CASE

History.—A girl, aged 7 years, was first admitted to the Mayo Clinic on May 4, 1928, because of attacks of extremely rapid cardiac action associated at times with syncope. She apparently had been in good health until eighteen months before, when she had been severely ill with pertussis. The only other infectious diseases she had had were epidemic parotitis and varicella. Tonsillectomy and adenoidectomy had been performed two years previously on account of slight impairment of hearing. Shortly after the patient had recovered from pertussis, a physician had detected the presence of cardiac arrhythmia and had advised a period of rest in bed. Special subjective symptoms had not been evident, and the patient had remained at rest for a few days only. A month later she had been examined again, and the physician had found a variation in the cardiac rate. The

rate at times was slow, at other times, rapid, and frequently the rhythm was interrupted by a "skipped beat." A few months later attacks of extremely rapid cardiac action had developed. These attacks had been of sudden onset, of variable duration and invariably had abrupt termination. The duration of the attacks had varied from a few minutes to several hours, and during the more prolonged seizures, especially when the rate of the heart had been unusually rapid, syncope had occurred. These attacks had increased in frequency and severity, and at the time of the first observations at the clinic were occurring several times a week. The attacks of syncope were not necessarily associated with the periods of cardiac asystole which occurred.

Examination.—The child appeared to be fairly normal; the state of nutrition was fair, and the color was normal. Results of general examination were essentially negative except for the cardiac abnormalities. The heart was not enlarged; the tones were normal, and murmurs were not audible. Great variations in the cardiac rate occurred over short periods of time. The systolic blood pressure was recorded as 80, in millimeters of mercury, and the diastolic pressure could not be estimated. Urinalysis did not reveal abnormalities. The hemoglobin was 75 per cent (Dare); the erythrocytes numbered 4,730,000 and the leukocytes 12,200 per cubic millimeter. The differential study showed 38 per cent lymphocytes, 0.5 per cent large mononuclear leukocytes, 4.5 per cent transitionals, 55.5 per cent neutrophils, 1 per cent eosinophils and 0.5 per cent basophils. The Pirquet cutaneous reaction was negative. The Wassermann reaction of the blood was negative. Roentgenographic studies of the chest showed the heart to be normal in size and contour. Electrocardiograms obtained during an attack of tachycardia revealed nodal (A-V) tachycardia. A diagnosis of paroxysmal nodal (A-V) tachycardia was made.

Treatment.—The child was admitted to the hospital for observation and treatment, where she remained for seventeen days. Quinidine sulphate, 65 mg., was administered every four hours, day and night. There was complete arrest of the paroxysms of tachycardia, but a slow nodal rhythm was established which continued through the period of observation.

After the child's return home, several attempts were made to reduce the amount of quinidine given, but the withdrawal of one or two doses invariably resulted in the return of the paroxysms. The pulse rate did not come within the normal range at any time. In September, 1928, the attacks again recurred, and the patient was again brought to the clinic for examination.

Second Examination.—Examination on September 24 revealed some loss of weight, and the child was restless and irritable. The heart was definitely enlarged; the total transverse diameter of cardiac dulness was 14 cm. The tones at the apex were accentuated and lacked the pure quality of normal tones. The rhythm was regular and the rate was slow. Roentgenographic studies of the chest revealed considerable enlargement of the cardiac shadow. Electrocardiograms showed the presence of slow nodal rhythm.

A period of moderately rapid nodal (A-V) tachycardia is shown in figure 1. The T waves in lead I were diphasic during this phase. The initial ventricular components of the electrocardiogram were essentially normal. Figure 2 represents continuous records obtained in lead I. The first two strips display short intervals of normal sinus rhythm and long periods of complete cardiac asystole. The onset of a paroxysm of nodal (A-V) rhythm is shown in the third strip. The termination of a paroxysm of nodal (A-V) tachycardia, followed by a remarkably long period of complete cardiac asystole, is shown in figure 3. This

is a continuous record obtained in lead II. The electrocardiogram shown in figure 4 was obtained five months later. Slow nodal (A-V) rhythm was present, with retrograde conduction. The P waves occurred just after the R waves and before the beginning of the T waves.

COMMENT

This case is of unusual interest from several standpoints. The occurrence of paroxysmal tachycardia in childhood is unusual, as evidenced

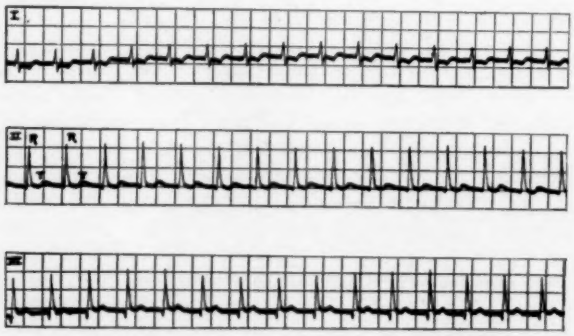

Fig. 1.—Electrocardiogram in all leads showing a paroxysm of nodal (A-V) tachycardia.

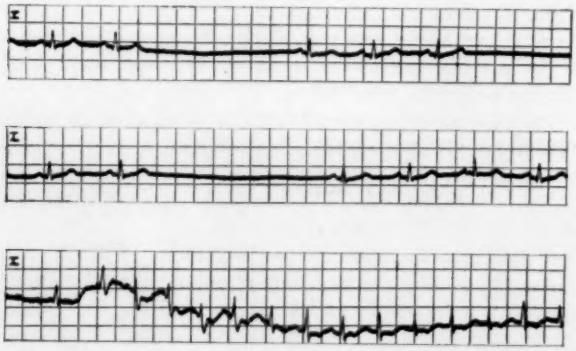

Fig. 2.—Electrocardiogram in lead I. The three strips are continuous and show periods of normal sinus rhythm, long periods of complete cardiac asystole and the onset of a paroxysm of nodal (A-V) tachycardia.

by the fact that the available literature records only twenty-four cases previously reported. The case forming the basis of this report is only the second case of paroxysmal nodal (A-V) tachycardia occurring in childhood.

The occurrence of syncope during the severe paroxysms of tachycardia was an alarming manifestation. The cerebral phenomena at

times attending paroxysmal tachycardia have been fully discussed by Barnes.[20] He found that the degree of symptoms varied from vertigo and temporary blindness to syncope and epileptiform convulsions. The symptoms are explained by cerebral anemia resulting from inadequate ventricular filling and hence inadequate ventricular output occurring as the result of extreme cardiac acceleration, especially when prolonged. Cerebral symptoms occurred most frequently when the origin of the impulse and its propagation in the heart varied the greatest from normal.

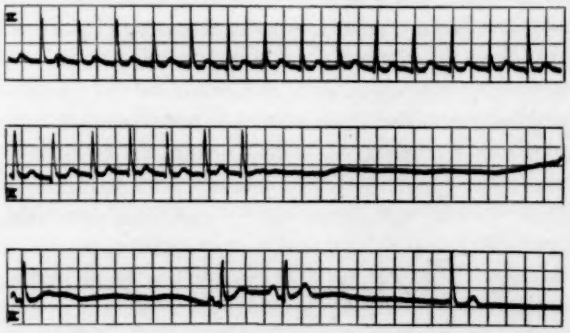

Fig. 3.—Electrocardiogram in lead II. The three strips are continuous. The termination of a paroxysm of nodal (A-V) tachycardia is shown, followed by an unusually long period of complete cardiac asystole.

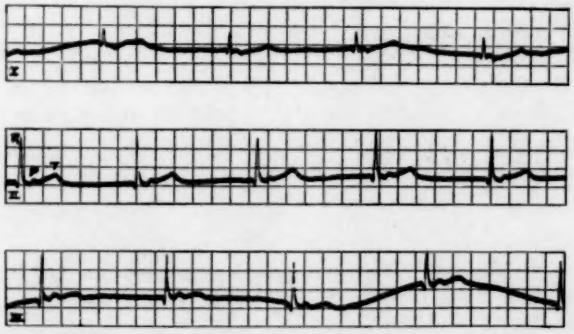

Fig. 4.—Electrocardiogram in all leads, taken five months after the electrocardiogram in figure 3. Slow nodal (A-V) rhythm, with retrograde conduction, is shown.

During the entire time of observation, even during the periods when the cardiac rate was slow, the resumption of normal sinus rhythm was not detected. Long phases of complete cardiac asystole occurred; they lasted as long as six seconds. They occurred independent of medication

20. Barnes, A. R.: Cerebral Manifestations of Paroxysmal Tachycardia, Am. J. M. Sc. **171**:489, 1926.

and independent of apparent injury to the paths of conduction. At this time we are unable to offer an adequate explanation of this extremely interesting phenomenon.

The partial control of the paroxysms of tachycardia by quinidine furnished additional data relative to the value of this drug in these disorders.

It is interesting to speculate on the etiology of the paroxysmal nodal (A-V) tachycardia in this case. The fact that three shifts in mechanism were recorded, nodal (A-V) tachycardia, slow nodal (A-V) rhythm and periods of complete cardiac asystole, accurately localized the underlying disturbance at or near the auriculoventricular node.

The fact that the heart was enlarged definitely during the five months which elapsed between our examinations established the existence of cardiac injury. Since the first cardiac symptoms became evident soon after an acute infectious disease, pertussis, we can hardly avoid considering this disease of etiologic significance. Such a relationship, if firmly established, would be of considerable significance in the nosology of pertussis. Hauser [21] described two cases in which, at necropsy, cardiac injury was disclosed occurring several months after pertussis. The salient pathologic changes included hypertrophy and failure of the left ventricle. In the one case in which microscopic study was undertaken, marked degenerative changes were not found.

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21. Hauser, Otto: Ueber Herzmuskelerkrankungen infolge von Pertussis, Berl. klin. Wchnschr. **58**:172, 1921.

IMPERFORATE ANUS WITH EXIT THROUGH PROSTATIC URETHRA

REPORT OF THREE CASES *

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Congenital anomalies often are of extremely practical as well as of academic interest. I have seen three cases in the past year in which there was no anus, and the child passed feces by way of the urethra. Imperforate anus alone is not extremely rare. The presence, however, of a urethral exit has been considered unusual. Zoehner [1] stated that rectal abnormalities occurred once in 25,000 births. It has been variously estimated by other observers that they occur even more frequently; some authors mention an incidence as high as one in 15,000. Recently Starr [2] reviewed the statistics and stated that rectal anomalies are found once in every 10,000 new-born infants. These figures include, of course, any abnormalities in the anus or rectum. A rather cursory examination of the literature shows that a urethral outlet is rare. Matusovszky,[3] in 1928, found only nineteen cases. I think that his statistics include largely the continental literature, as I have been able to find three additional cases in articles recently published in this country.

The three cases, which I will present, all came to postmortem section. Dr. Wahl, of the University of Kansas, furnished the data for one case; Dr. F. G. Bartell and Dr. Wahl, that for another, and Dr. J. G. Montgomery that for the third. All three cases were investigated in the department of pathology at the University of Kansas, and all occurred in the period of one year.

REPORT OF CASES

CASE 1.—G. R. was born with an imperforate anus, and a colostomy was performed when he was 2 days old. He did fairly well, but was brought to the hospital when 2 years of age with a fecal impaction; an artificial anus was made. Two months later the sigmoid was anastomosed to the colon leaving the colostomy open. The child went home to rest, but returned to the hospital with

* Submitted for publication, April 18, 1929.

* From the Department of Pathology, the University of Kansas, and St. Luke's Hospital.

1. Zoehner, quoted by Matusovszky: Zentralbl. f. Gynäk. **52**:496, 1928.

2. Quoted by Landsman, A. A.: Report of a Case of Absence of the Anus and Imperforate Rectum Complicated by Congenital Recto-Vesical Communication, Tr. Am. Proct. Soc. (1927) **28**:19, 1928.

3. Matusovszky, A.: Ein Fall von Anus urethralis, Zentralbl. f. Gynäk. **52**:496, 1928.

a distended abdomen, and died in a few days at the age of 2½ years. At the necropsy the artificial anus was not functioning well. The large intestine showed a typical Hirschsprung type of megacolon with marked fecal impaction. An anastomosis was present between the colon and the sigmoid, and a communication was discovered between the rectal pouch and the prostatic urethra. The right ureter and pelvis of the right kidney were widely dilated. The parenchymatous organs showed some cloudy swelling.

This case was interesting, as it showed that at least one of the possible factors in the formation of a typical Hirschsprung's disease is that of stenosis and that the urethral outlet could not take care of the fecal material.

CASE 2.—This patient was sent in by Dr. Bartell, who had removed the organs and had made a preliminary report of his observations. The history stated that the child at birth had no anus and passed flatus through the urethra, and that the diaper was stained with fecal material. An artificial anus was attempted on the second day after birth. The rectum could not be located. A colostomy was then performed. The child did well for about a month and then declined rapidly, showing some fever and marked dehydration. He died at the age of 4 months, extremely emaciated and dehydrated. At autopsy an anal dimple was found. The colostomy had healed nicely. The large intestine was markedly contracted and ended in a blind pouch, with a band of connective tissue, which had no lumen, connecting the blind pouch with the anal dimple. There was a small communication between the rectal pouch and the prostatic urethra. An interesting incidental observation was a typical horseshoe kidney. It might be mentioned here that congenital anomalies are frequently multiple.

CASE 3.—G. H. was born seven months prematurely. Delivery was normal but the child had no anus; not even a postanal dimple was found. The infant passed both feces and urine by way of the urethra. He did not do well; hence, when he was about 1 month old, a colostomy was done. For about ten months his progress was excellent, but about this time it was found necessary to dilate the colostomy opening frequently. He again entered the hospital at the age of 2½ years, with a history of fecal vomiting. There had been a gradual and progressive emaciation for several months, and he was still passing both urine and feces through the urethra. He died in a state of extreme emaciation and dehydration. At postmortem examination the colostomy opening was found to be patent. There was some dilatation of the colon below this, and the bowel ended in a blind rectal pouch about 1 cm. from the anal dimple. There was a communication between the prostatic urethra and this rectal dilatation through which feces could be readily expressed. All other visceral organs showed marked starvation atrophy.

COMMENT

Many different types of rectal anomalies have been described in which the rectal pouch communicated with other pelvic viscera. Vulvar anus is sometimes seen in the female; it has also been found to open high up in the vaginal canal. Abnormal openings on the surface of the skin have likewise been reported, as, for instance, when the anus is found at the root of the penis.

Naturally such unusual malformations bring up the question as to the embryonal defect responsible for such anomalies. Wood-Jones [2] believed that "They arise from an irregular, or arrested development of the proctodeum and postallanotic gut, with or without persistence of communication with the cloaca." He gave five different characters which may be enumerated as follows:

First, invagination of the ectoblast at the anal site does not take place.

Second, rudimentary invagination, but anus remains imperforate and anal membrane persists in whole or part.

Third, postallanotic gut undeveloped, does not descend and ends blindly.

Fourth, postallanotic gut descends but grows backward and remains out of alignment with the proctodeum and the intervening tissue not absorbed.

Fifth, growth of cloacal partition is arrested and communication is made between rectum and parts in front of it.

All the cases I have presented showed the same picture. In all three cases operative intervention was attempted; in none of them, however, was it successful except as a temporary expedient.

All the patients died showing practically the same picture of dehydration and emaciation.

As for operative intervention, as far back as 1907, Ashurst [4] showed that in the majority of cases the rectum could be reached by the perineal route. He said that "In only three out of twenty-two cases in which the rectum was not found by the perineal incision, and which are reported in sufficient detail, would it have been impossible to reach the rectum by the lower route." This seems to be the general consensus of opinion among most surgeons. In cases such as I have presented in this discussion, however, the communication with the prostatic urethra brings into account a secondary factor which would affect the prognosis. All three of the patients whose cases are reported in this paper showed the rectum ending in a blind pouch at a considerable distance from the anal dimple; this would have made the operation more hazardous than the sometimes rather simple opening through an imperforate anus into the rectum.

CONCLUSION

Three cases of imperforate anus with communication and excretion of bowel contents into the prostatic urethra are presented. In all three cases the condition was not permanently relieved by operative intervention. One child died at the age of 4 months and the other two at the age of 2½ years. One patient showed a typical Hirschsprung megacolon demonstrating one of its possible etiologic factors. Without the complicating urethral communication, the condition in the majority of cases is relieved by operation. This complication apparently renders a more serious prognosis. In one of the cases, temporary relief was obtained by means of colostomy.

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4. Ashurst: Univ. Penn. M. Bull. **20**:96, 1907-1909.

ECTOPIA CORDIS *

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The literature on ectopia cordis consists largely of case reports. Few statistics concerning the incidence of the malformation are available. Maude Abbott [1] listed seven instances in 850 cases of congenital heart disease. In the report of an example in an infant, aged 15 months, in 1919, Holmes [2] stated that such anomalies were by no means rare. For some, the abnormality is merely one of anatomic interest. But most people seeing this condition for the first time will feel with Greig [3] that "cleft sternum associated or unassociated with ectopia cordis is sufficiently rare to appeal to the imagination as an extraordinary occurrence."

Only recent papers dealing with the subject need be cited. Cutler and Wilens,[4] in 1925, reported a case of pectoral ectopia cordis and reviewed the recent literature. In 1926, Greig [3] described a case showing absence of the sternum, reviewed much of the older literature, and discussed at length questions of embryology. In the following year, Bloch [5] reported an interesting case of pectoral ectopia with absence of the sternum. The opening in the skin was enlarged, the heart "sunk" and the skin closed over. This procedure caused a standstill of the heart, and the organ had to be brought back to the surface. Although infection developed, the child was kept alive for eight days. Necropsy revealed no further abnormalities.

In most cases of ectopia cordis, structural defects in the heart are also present. In the case to be reported, malposition of the heart was the sole abnormality of that organ. Moreover, the sternal defect was smaller than in most of the reported cases of the pectoral type of ectopia. This may be of interest from the standpoint of embryology. From Cruveilhier's clinical description, the present case appears similar to one he [6] reported in 1841, of which he said the heart of the infant was

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* Submitted for publication, April 1, 1929.

1. Abbott, Maude, in Osler: Modern Medicine, Philadelphia, Lea & Febiger, 1927, vol. 4, p. 654.

2. Holmes, J. B.: Ectopia Cordis, with a Report of a Case in a Fifteen-Month-Old Infant, Johns Hopkins Hosp. Rep. **18**:287, 1919.

3. Greig, David M.: Cleft Sternum and Ectopia Cordis, Edinburgh M. J. **33**:480, 1926.

4. Cutler, G. D., and Wilens, G.: Ectopia Cordis; Report of a Case, Am. J. Dis. Child. **30**:76 (July) 1925.

5. Bloch, Sophie: Ein Fall von Ectopia cordis pectoralis, Zentralbl. f. Gynäk. **51**:625, 1927.

6. Cruveilhier: Note sur les mouvements et sur les bruits du coeur, Gaz. méd. de Paris **9**:497, 1841.

placed out of the chest, from which it had entirely escaped through a circular perforation in the superior part of the sternum.

REPORT OF A CASE

The infant's mother, a primipara, aged 25, had had poor health for many years. The appendix was removed in 1920 and an ovarian cyst, in 1923. During 1924 pleurisy with effusion developed, and the patient spent some time in a tuberculosis sanatorium. Because of menorrhagia, the uterus was curetted in 1925. During the same year tonsillectomy was performed; this was followed by multiple arthritis. Two developmental anomalies in the mother had been revealed by roentgen examinations; the twelfth rib on the right side was absent and that on the left was rudimentary; the pyelogram showed a double kidney pelvis on the right side. Edema of the legs began early in pregnancy, and because of uterine bleeding severe anemia developed. During the night of Aug. 9, 1928, when the mother had come about to term, there was a severe uterine hemorrhage, following which the

Fig. 1.—Appearance of infant with ectopia cordis, after death had occurred.

hemoglobin fell to 29 per cent. A diagnosis of placenta praevia was made, and the next morning Dr. C. W. Webb performed a cesarean section.

The infant was fully developed and well nourished. It began to breathe promptly after delivery. Aside from the malposition of the heart, it appeared normal. An attempt was made to enlarge the opening in the thorax and place the heart inside, but it soon became obvious that this could not be done. The position of the heart is indicated in figure 1. Both auricles and ventricles were entirely without the body cavity. The heart was thrown backward and to the right, so that the apex was under the chin; the posterior surface was directed upward. The sequence of contraction appeared normal and, in addition, with each systole there was a forceful movement of the heart as a whole, a sort of recoil. The rate of beating was about 115 a minute. Two hours after birth the rate fell to 18 a minute, and it seemed as though the heart would stop. After a little warm physiologic solution of sodium chloride was poured over the heart, it recovered and continued to beat at the rate of from 100 to 110 for about eight hours, when it gradually became slower. Most of the time the infant's color was good. Its cry was feeble. Clear blood-tinged mucus exuded from the mouth at

intervals during the day. The body was quite cold even when not cyanotic. The child lived for sixteen and a half hours. No special measures were taken to prolong life.

At the postmortem examination, the body weighed 1,730 Gm. No abnormalities were found except those related directly to the ectopia. When free from blood, the heart weighed about 15 Gm. In the longest diameter from apex to base, it measured 7 cm. The transverse diameter was 6 cm. The parietal pericardium was present only at the pedicle where it was reflected from the great vessels and became continuous with the skin. There were no anatomic defects in the heart itself, and the great vessels were normal.

The sternum is shown in figure 2. At the site of the manubrium was a circular opening 2.5 cm. in diameter, which was incompletely closed above. The attachment of the clavicles appeared to be normal. The sternal defect is of particular interest as it is much smaller than is usually encountered in such cases.

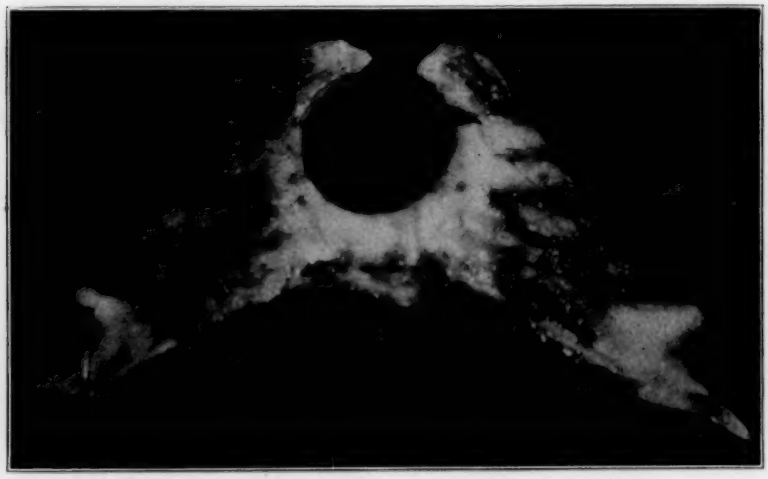

Fig 2.—Appearance of sternum.

According to Keith,[7] no satisfactory embryologic explanation has been given for this condition. In cases of cervical ectopia there is failure of the heart to descend into the thorax, but in pectoral ectopia the primary defect is a sternal one. N. W. Ingalls[8] has suggested that the actual primary defect may be in the anterior body wall and that the sternum is defective for this reason. Considering the present case, he thinks that one must assume failure of the ribs and sternum to grow ventrally toward the midline in front of the heart; but he points out that it might not be possible to distinguish between primary failure of the halves to unite and a consequent ectopia or, on the other hand, some malposition of the heart itself which prevented the ribs and sternum from growing ventrally. He inclined to the latter view, since there was a good attempt to unite the two halves of the sternum both above and below, which was more successful in the lower part.

7. Keith, Arthur: Human Embryology and Morphology, ed. 4, New York, Longmans, Greene & Co., 1921.

8. Ingalls, N. W.: Personal communication to the author.

An electrocardiogram taken with the usual standard limb leads ten hours after birth is shown in figure 3. The interpretation of these curves is, however, doubtful. The large wave occupying the position of T which is characterized by a sharp and rapid descent certainly extends beyond the duration of systole, so that there is no electrical diastole, although the rate is only 87 beats a minute. It seems possible that these waves are in some way due to a mechanical factor con-

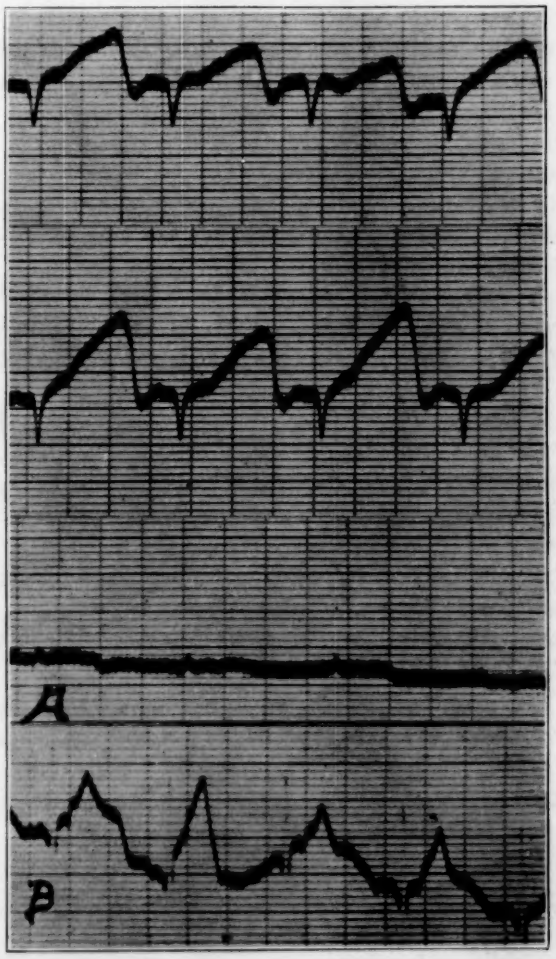

Fig. 3.—*A*, electrocardiographic tracing from the usual limb leads. *B*, direct lead from the midsulcus region.

nected with the recoil of the whole heart which occurred at the end of systole. Semidirect leads were taken with one electrode attached to the left leg and the other electrode (right arm lead) placed on the surface of the heart over the various chambers. But as only one galvanometer was available, simultaneous records with standard leads could not be taken, and it was impossible to separate accurately the intrinsic and extrinsic deflections recorded from such leads. Large

T waves similar to those seen in the indirect leads were recorded. From the mid-sulcus region, an apparently normal ventricular complex was obtained (fig. 3 *B*), but this may be merely an accidental observation.

SUMMARY

A case of ectopia cordis is reported. No abnormalities in the heart itself or in other organs were found. The sternal defect consisted of a small, circular opening in the manubrium. Electrocardiograms were obtained, but their interpretation is doubtful.

ACUTE MASTOIDITIS IN AN INFANT AGED EIGHT WEEKS *

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Within the last few years there has been an intense interest in otologic infections in early infancy due, in a great degree, to the work of Marriott on mastoiditis in young athreptic infants. There has been a general feeling, however, that the association of vomiting and diarrhea, on which so much emphasis has been placed, was possibly not an essential part of the picture. Also in some quarters it was felt that even the existence of a definite clinical and pathologic mastoiditis at so early an age was open to question. About a year ago, I reported [1] a case of mastoiditis in an infant, aged 10 weeks, as a postmortem observation without any of the usual signs or symptoms. I now wish to report the case of a patient with mastoiditis who was operated on at the age of 8 weeks; undoubtedly, the condition was of even earlier origin. It was the work of Marriott that gave me courage to make the diagnosis and submit the child to operation. The clinical history in this case is the typical history of an acute mastoiditis, and the operative observations are definite. The slight variations from the course of the disease in older children are only those dependent on the difficulties of accurate observation of the ear at this age.

It is worthy of note that the severe and persistent vomiting in this case was of an origin completely and demonstrably separated from the otologic complication, and the occurrence and subsidence of this complication had absolutely no effect on the underlying condition. At no time was there any tendency to diarrhea, and there were no symptoms referable to the mastoid except the temperature and the local observations. The anatomic possibilities of a mastoiditis in the infant, I believe, are now generally fairly well conceded, and although the antrum is small, it is sufficiently differentiated to give rise to the classic picture.

REPORT OF CASE

D. O., a white boy, born on Dec. 12, 1928, after a normal full-term pregnancy, weighed 8 pounds (3.6 Kg.); the delivery was normal, without instrumentation. He left the hospital on the tenth day, weighing 7 pounds and 13 ounces (3.5 Kg.). He was a first child, and there had been no miscarriages. He was breast-fed for two weeks, and then was given a milk, water and sugar mixture, about 50 calories per pound. He was brought to the office at the age of 6 weeks because of per-

* Submitted for publication, May 4, 1929.

1. Silver, H. B.: Acute Occult Mastoiditis at Ten Weeks, Laryngoscope **38**:45 (Jan.) 1928.

sistent vomiting and loss of weight. He had vomited some since birth, but the vomiting had markedly increased within the last two weeks. The stools were dry and small but contained fecal matter; there were from one to two stools a day. The child was somewhat dehydrated. There was a marked generalized hypertonia. The fontanel was normal. There was no abdominal tumor or peristaltic wave. He weighed 6 pounds and 10 ounces (3 Kg.). He was put on lactic acid whole milk and Karo syrup, about 85 calories to the pound. He was brought to the office in four days, the weight being 6 pounds and 13 ounces (3.1 Kg.), but the vomiting seemed worse and at times was projectile. On account of the marked hypertonia and the absence of a peristaltic wave or an abdominal tumor a diagnosis of pylorospasm was made, and the patient was admitted to the hospital. A diet of lactic acid milk thickened with cereal was continued with the addition of subcutaneous dextrose solution and atropine sulphate 1:1,000 solution up to 3 drops before each feeding. At this dosage definite signs of atropine poisoning appeared—fixed dilated pupils, dry mouth, flushed skin and a rise in temperature. The use of atropine was then stopped and thickened feeding alone was given. On three other occasions, the administration of atropine was followed by a sharp rise in temperature which dropped when the drug was discontinued.

Ten days after admission, the child began to run an irregular temperature. Examination at this time revealed a marked redness in both ear drums, more marked on the right side, and a bilateral myringotomy was done. The left ear gave a dry tap, but a small amount of pus escaped from the right ear. Irrigation of the right ear for twenty-four hours gave some shreds, but after that the return was clear. Four days after the myringotomy, as the temperature was then definitely septic, varying daily from almost normal to 105 F., the patient was seen again in consultation by the otolaryngologist, Dr. Barkhorn. The drums and canal were apparently normal, but because of the pus originally obtained on myringotomy and the lack of any other cause for the rise in temperature a bilateral mastoidectomy was decided on. The child was operated on on the following day by Dr. Barkhorn, and the observations were as follows:

With the patient under local anesthesia, the right mastoid tip was opened and immediately under the cortex free greenish pus was found. The mucous membrane of the antrum and a greater part of the bony wall had undergone necrosis. The process extended upward and forward, involving the whole of the mastoid process and the underlying bone. This was curetted and drained. The left mastoid was opened and was normal except for a gelatinous fluid and a swollen mucous membrane. Cultures were taken and reported: The right ear showed staphylococcus, pneumococcus and a gram-negative bacillus resembling proteus; the left ear showed a scanty growth, gram-positive cocci which were large but probably not pathogenic.

During all this time the child vomited severely, holding its weight only with difficulty. It was expected that after the operation the vomiting would cease. After a stormy convalescence, however, the mastoid wounds healed nicely but the vomiting persisted and was even worse. After a further trial of thickened cereals and atropine (which was discontinued on account of toxic symptoms) the child did poorly but the extreme hypertonicity disappeared. When relaxation occurred it was possible to make a satisfactory abdominal examination and a definite pyloric tumor was felt. On March 26 (thirty-eight days after the mastoidectomy), Dr. H. B. Epstein did a modified Rammstedt's operation; the vomiting ceased promptly and the infant went on to complete recovery and discharge twelve weeks after admission.

COMMENT

I was able to present a case of proved mastoiditis in an infant, aged 8 weeks, which was not a terminal manifestation, with operation and recovery.

The fact that although the condition occurred in the presence of congenital hypertrophic pyloric stenosis it apparently in no way affected the course of this disease is of interest.

I also wish to call attention to the repeated attacks of atropine fever with their prompt subsidence on the withdrawal of the drug.

Progress in Pediatrics

CONSTIPATION AND BEHAVIOR*

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Sir William Arbuthnot Lane regarded as sound doctrine the view of the New Zealand Maori that when the bowels are clean the whole body is clean. And he made the comment: "Its ethical significance is far wider and greater than most of us imagine. The connection between the nervous system of the abdominal and pelvic region and that of the brain is so close and intimate that literally it is a fact that the state of mind and even of the character is largely governed by the state of the bowels." One need not accept this dogmatic statement nor Lane's ideas concerning chronic intestinal stasis; namely, "The whole body gradually becomes saturated with bowel poisons and this poisoning produces physical disease, mental depression and disorganization, and frequently moral disorder as well."

There is little doubt that many primitive people, including the Maori, gave much attention to the bowels and placed various emphases on dietetic regulations to insure adequate intestinal action. The basis of this activity was in part due to the belief that, "When anybody felt out of sorts they said the 'inner man' was unhealthy and out of order." The Maori are said to have included in their ideal of life the satisfaction of three soft stools daily.

Throughout the ages a relation has been assumed to exist between constipation and mental aberration, particularly in the forms of melancholia and depression. James Harvey, writing in 1706, in "Praesagium Medicum," commented, "If we can't account for the Union of the Mind and Body, nor reach it with the Eye of our Reason; yet the mutual Sympathy that's between them is very dubious; For, while the Blood and Spirits run briskly in their Channels, the Mind is pleased and joyful; But, when they are slow and dull or obstructed in their Motions, we are sad and pensive; And upon the least Indisposition of the Body, our Mind is put into Disorder and Perturbation."

Archibald Pitcairn more definitely wrote in 1627, "Hypochondriac Distemper, is a Disease of the Intestines *without the animal.* The Hysterical Affection is of the same Nature as the Hypochondriac." One might quote numerous authorities of the past and present favoring a belief in the definite dependence of physical and mental disorders on constipation.

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* Read at the Sixth Annual Meeting of the American Orthopsychiatric Association, New York, Feb. 22, 1929.

What constitutes constipation? Dr. Lauder Brunton regarded constipation as one of the commonest troubles of civilized life, that "occurs so frequently in people who are otherwise perfectly healthy, that to a great extent it must not be regarded as a disease but as the natural result of artificial conditions acting upon a healthy body." The large majority of people regard constipation as a definite disease state. At the highest valuation, it should be regarded as a symptom and not as a disease entity.

Many persons define constipation as an abnormal state of being, irrespective of its causation. Constipation is essentially a diminution in the amount or frequency of bowel movements. Activity of the bowels and the amount and nature of the stools present frequent variations in health. Some persons are comfortable with evacuations once a week or every three or four days, while others appear to require daily evacuations regardless of quantity or quality.

Tuttle stated: "Constipation consists in the passage of insufficient amounts, or the abnormal prolonged retention, of fecal material in the intestinal canal. A healthy individual passes upon an average of six ounces of feces in twenty-four hours. These figures, however, are only relative. . . . It requires from 15 to 20 hours for the food to pass through the intestinal canal. The ordinary assumption based upon these figures is that every normal individual should have a stool of adequate quantity once in 24 hours. So imbued with this idea are the laity in general, that one who does not succeed in having such a passage, or whose passages do not appear to be normal in quantity, quality, color or consistence, immediately considers himself the victim of constipation and begins to take drugs or enemata to remedy the condition."

Kemp expressed the belief that "healthy persons usually have one bowel movement daily, generally about the same hour. Some normally have two actions a day while others empty the bowels every other or every second day and yet are in perfect health."

If constipation is not a disease but a symptom, it is obvious that it may be a manifestation of a functional or organic disease. Generally speaking, constipation arises from lessened expulsive power or increased resistance to evacuation. Hence, it may depend on alterations of the nerve supply or occasionally on disorders of central origin, such as melancholia, mania and the like, but most frequently it has a reflex origin or is due to some peripheral action on the intestinal nerves. It is patent that constipation is related to conditions causing intra-abdominal tension or fecal retention, such as may arise from abdominal tuberculosis or from peripheral irritations due to piles, fissures and ulcers. Inadequate diet necessarily affects stools. Too much bulky and indigestible food may cause diarrhea, with constipation as a protective

reaction against it. This, incidentally, is also the effect of using purgatives. Constipation is likewise the result of what has been termed "A nervous torpor due to habit." The disregard of the irritation of the rectum that indicates the necessity for evacuation leads to a diminished sensitiveness to this stimulus and thus promotes irregularity in the habit. Even preoccupation of the mind by thoughts or emotions definitely interferes with stools.

Whether one talks in terms of sluggish bowels, deficient absorption of intestinal juices or of the too rapid absorption of fluids passing through the colon, it is evident that the food habits play a part in the causation of constipation. Constipation in turn, for one reason or another, exercises a definite influence on the nature and extent of the daily dietary.

Reflex irritations inhibit peristalsis, and intestinal obstruction from whatever cause conduces to sluggishness of the bowels, but much of what is termed constipation arises from inadequate dietetic habits, an insufficient appreciation of the needs of obeying the ordinary calls of nature, or interference with natural action of the bowels.

Chronic constipation from impaired physiologic function is at times classified as a motor neurosis. Kemp referred to the atonic form of constipation due to neglect of the call of nature and to the spastic form that results from depressing emotions. He did not hesitate to say "Worry and mental strain have an influence and it (constipation) occurs among neurasthenics and hypochondriacs."

Heredity probably plays little part in constipation, as most constipation arises from habits of living, carelessness in attention to the activity of the bowels and more especially to the continuous and increasing use of laxatives, particularly when such administration is begun during childhood. The very fact that so much attention is given to the evacuations of children is responsible for a common type of experience in succeeding generations that leads some persons to believe in an hereditary tendency toward sluggishness of the bowels. Especial attention is given to constipation in childhood. Infants are more susceptible to symptomatic constipation than children of 2 years and older, largely because of possible malformations of the intestine in the form of narrowing, because of difficulties in artificial feeding and even because of an insufficiency of lactose in the mother's milk. Stress on concentrated milk diets has increased the likelihood and prevalence of constipation.

There are children who manifest sluggish action of the bowels almost from the time of birth, but who would achieve a normal fecal equilibrium if it were not for interference with normal processes. Constipation is not a common symptom among children between the ages of 3 and 12 years, but is more likely to become manifest during the adolescent period. This is in part due to the development of those false

modesties which at times hamper the recognition of calls of nature and bring about a neglect of conservation or formation of habits. Absorption in school, in social affairs, and indeed in open air sports, in which both sexes participate, also conduces to a larger degree of costiveness during the adolescent period.

A still more important factor, however, in the causation of constipation and in the production of symptoms incidental to constipation lies in the social stress that is placed on the necessity for daily stools. The bowels constitute an important topic of conversation in the home. Habits of bowel movement provide a large measure of public interest, if one may thus interpret the broad field of advertising of laxatives in the form of foods, fruits and salts, and the extensive presentation to the public of the values of various forms of baths, irrigations and treatments that vary from the "apple a day" to the denials of Christian science. The degree to which regulated intestinal action is dependent on formation of habits and training indicates that there is a social factor in bowel activity, because the standard of evacuation which serves as the measure of daily adequacy assumedly is based on human experience. The infant certainly is not aware of the social codes regarding stools, nor is he cognizant of the social necessities of evacuation in terms of time, place and circumstance. He depends on physiologic function regardless of its modification by organic or dietetic difficulties. He must be conditioned in social living.

Fecal movements, while to some extent involuntary, are largely determined by education and formation of habits. One can accustom the bowels to move once daily, three times a day, or once in four or five or more days. In general, persons in whom evacuation occurs with some degree of regularity every three days or even once a week are just as healthy as other persons whose bowels function mornings and evenings. In illustration of this, I may perhaps call attention to a few striking illustrations.

Tuttle reported a patient whose bowels moved once in twenty-eight days at the full of the moon. Matthews described a person whose fecal movements occurred once in two weeks and were gradually extended so as to occur once in four months. There are many interesting, though of course anomalous, experiences recorded of patients whose bowels moved as infrequently as once in six months, a year or even longer times. I have observed a strong, vigorous, active negro, who while under observation and control had a single movement of the bowels in two months. He suffered more from the idea that he was different from other people than from his profound but not enervating constipation. He was more distressed by his social deviation than by any other factor in his daily life.

It is unnecessary for me to dwell on the physiology of intestinal activity, or to refer to the sacral nerves, the hypogastric plexus and the

ganglionic sympathetic fibers which are involved in intestinal innervation. It is necessary, perhaps, to recall that the vagus stimulates intestinal movements while irritation of the splanchnics arrests them; however, even these reactions may be reversed. The intestines constitute an automatic mechanism which is regulated by, but not dependent on, the intrinsic nerves. Peristalsis in the small intestines is influenced by impulses arising from the upper part of the alimentary canal; hence, there is a definite relation between the time the stool is passed and such events as the taking of food, a glass of water, a cup of coffee or smoking. A regular stool immediately after breakfast indicates the degree to which this upper alimentary stimulus causes defecation as a habitual response.

The peristaltic action is influenced by sensations and emotions, particularly such as anger and fear.

Ordinarily, food requires eighteen hours from the time of ingestion to its arrival in the rectum. The rectum normally is empty immediately prior to defecation, and it is the movement of the feces into the rectum that creates the desire for evacuation. Generally speaking, if the bowels move daily the interval between the meal and the evacuation of its undigested residua varies from nine to thirty-two hours. If the desire to evacuate is resisted, it soon passes away and there may not be a recurrence for twenty-four hours or longer.

In the infant, the bowel movements are involuntary. The earliest education brings about a series of efforts at conditioning as a result of which early control over the sphincter may be secured. The processes of voluntary defecation are initiated by stimuli varying from the insertion of a soap stick or of placement on a vessel to massage of the abdomen. This conditioning process is most useful during the first year of life. The voluntary control of evacuation for the vast majority is practically established by the eighteenth month of age.

It is recognized that mental states definitely affect peristalsis. Fear increases peristalsis and may cause evacuations that are wholly involuntary. Repressed emotions such as anxiety and grief lower the degree of nervous activity and may bring about varying degrees of sluggish peristalsis manifested as marked constipation. Fear of evacuations postpones them; fear of no evacuation leads to interferences that hamper natural defecation.

I do not purpose at this time to dwell on the states of physical and mental health and their resultant behaviors arising from organic causes. The effect of tumors, intestinal bands and specific diseases of all sorts are of importance, but the symptoms that exist in these conditions are modified by the underlying pathologic state. I desire at this time to refer to some forms of behavior in which constipation is a marked symptom and in which the social stress on the stool is far more important than any physical influence and any primary psychologic factor.

SYMPTOMATOLOGY

The symptomatology of constipation, if it is considered as a disease, is a question of importance, but I am more interested at present in constipation as a symptom. There is a sharp distinction between the effects of constipation considered as a psychologic entity in itself and as a secondary factor which only by virtue of its continuance assumes the force and influence of a primary condition. Lynch commented: "The symptoms of constipation are numerous and varied, and nearly every disease that man is heir to can be traced to the condition of his bowels." This, of course, is too specialistic a statement and is as much an overstatement as the views of Lane with reference to the effects of intestinal kinks on morals. While Lynch referred to constipation as etiologic in insanity, he also attributed vertigo, asthma, diseases of the heart and kidneys, menstrual disorders and gout as well as eruptions of the skin to constipation. He gave reason for careful thought when he added, "The writer is convinced after years of special work in this line, that more hypochondriacs and neurasthenics are created by a lack of daily movements than by almost any other condition." I am forced to ask whether hypochondriac and neurasthenic persons were created by lack of daily movement or by dwelling on the fact that a daily movement is the social standard to which all persons are expected to conform.

Certainly the demand for, and often the social insistence on, daily catharsis leads to an attempt to secure this routine performance by the use of special dietaries, enemas, abdominal massage, colonic irrigations and drugs. Such social physiology is responsible not merely for induced evacuations, but for a large assortment of symptoms dependent on an oversolicitude for intestinal action and an astigmatic mental attitude toward what should be a simple physiologic phenomenon. A distortion of the social meaning of the biologic act of defecation has resulted. The cathartic habit is established on the basis of social necessity rather than on biologic demand. The very efforts at inducing social conformity with routine stools are responsible for the existence of much constipation. The series of reactions incidental to the artificial physiologic activity, plus the overcompensating psychologic interest in defecation are distinctly disadvantageous. There is no necessity for creating a hypothesis based on anal eroticism. The biologic social conflict is wholly sufficient to explain the resultant behaviors.

In many children, the lack of a daily stool does not produce physical or mental distress. If occasionally a desire to evacuate the bowels is ignored, the impulse may pass away without any feeling of discomfort in the abdomen or any resultant lassitude or headache. Occasionally a child, of its own initiative, may complain of discomfort. If the bowels are constipated for several days or a longer period, the hardened feces may cause an intestinal irritation with a resultant diarrhea that serves

as a relief from the constipation. An actual catarrhal colitis may result or there may be any one or more of a group of symptoms, including anorexia, furred tongue, halitosis, colicky pains, jaundice, irritability, depression, headaches, temper, mental depression and even intellectual slowness. Prolonged obstinate constipation has been held responsible for a variety of more serious cerebral disturbances including some that I have already mentioned, as giddiness, hypochondriasis, melancholia and mania.

Some persons present a variety of nervous reactions and may actually be in a more or less impaired state of health from the secondary effects of constipation. Such persons are frequently described as being thin and spare, with pimply or muddy complexion, and often have dark circles under the eyes. They frequently evidence a more or less hypochondriacal condition combined with a disinclination for mental exertion. Vertigo and headache are probably no more common than flatulence and borborygmus. The feeling of weight and fulness after eating and a lack of appetite are paradoxic elements.

Children, particularly, evidence restlessness, some distention and tenderness of the abdomen and occasionally a rise of temperature. In severe cases there may be palpitation, dyspnea and even convulsions. In the long continued types, anorexia, restlessness and irritability are dominant factors accompanied at times by attacks of vomiting and abdominal pain.

The physical effects are thus a sense of weight and fulness and poor appetite, all arising from a retained mass of food. Flatulence and borborygmus arise from states and degrees of fermentation. Toxic absorption may give rise to dulness, malaise, headache and convulsions, any or all of which are spoken of as autointoxication. Local irritations may cause jaundice, colitis and pain. All of these physical elements are accompanied by or cause psychologic reactions which enter into behavior.

Buckley commented that "sluggish bowels are more often present than absent in dementia praecox." Referring to chronic intestinal stasis, he remarked that in many instances physical conditions are found which do not produce the existent symptoms, but that in a person of the deviate type these physical conditions furnish the contributory element among the combined biologic factors that must be removed. I may add that the physical conditions are probably no more important than the psychologic conditions which dominate the picture of the secondary effects of sluggish intestinal action.

Adler, from his point of view of constitutional inferiority, and the masculine protest, stated, "A number of neurotic symptoms, such as erythrophobia, neurotic obstipation and colic, asthma, probably also vertigo, vomiting, headache and migraine stand in some sort of relation, which is as yet not entirely clear to me, with a voluntary but uncon-

sciously cooperating activity of anus contraction, and that of abdominal pressure, symbolic acts which are accomplished through the domination of the reinforced fiction." It is unnecessary to dwell on Adler's idea of fictitious goals to appreciate some of the relationship that exists between the symptoms of neurotic behavior that he mentioned and constipation as a unit symptom. There is a definite linkage in the symptomatology as an expression of a conflict between biologic and social adaptation. A large portion of the symptoms are explainable on the grounds of suggestion, personal and social, heterosuggestion and autosuggestion. No one doubts that habits of bowel movement have definite relationships to mental status and attitudes, to social demands and education, to personal attention and to social training. It is perhaps difficult to differentiate the symptoms that grow out of constipation per se and those attributable to the social components that arise from parental and pedagogic efforts at inducing what are deemed adequate habits of stool.

For the purpose of classification of behavior types as related to constipation, I must differentiate two main sets of reactions, namely, those which arise from physiologic factors incidental to intestinal inactivity and those inherently the result of social attitudes. A feeling of weight in the abdomen and a sense of distention or subacute pain may be definite effects of constipation and may result in physical sluggishness and inactivity. A fear that has resulted from the fact of nonevacuation cannot be attributed to purely physical causes, though the purposeful nonevacuation due to fear of pain from a rectal ulcer has a physical origin. The attitude toward stools and the fears concerning the effects of constipation are instituted by social guidance. Physiologic organization does not dwell on the hazards of constipation and the dire effects of sluggish bowels on general welfare. The centering of interest in cathartics and enemas and an almost constant solicitous interest in bowel action are not inherent physical responses but result from a social component which has been related to intestinal activity.

CONSTIPATION IN CHILDREN

Among children, one notes types of behavior which may be crudely divided into several groups. The first type evidences no physical distress, even though the bowels move only once a week, and these children do not find the weekly cycle a source of physical or psychologic discomfort. They do not individualize social behavior in terms of their essential deviation from the social norm. Children of this type may be regarded as being in biologic social equilibrium, without a physiologic or psychologic deviation from normal behavior, except the single fact of constipation.

In the second type, the social factors appear to dominate the biologic factor. The parental solicitude or the stress placed by the teacher or

the camp director on habits of bowel movement transforms a normal physiologic rhythm into a biologically abnormal routine with the concomitance of a variety of psychologic disturbances. The social pressures are in dominant conflict with the physiologic activities of the child. Among this group one finds a large variety of neurotic manifestations, hysterias, negativism and phobias with the resultant familiar types of behavior.

The third group involves again the biologic social factors but with the greater stress placed on the physiologic component. There is inherent more evidence of the self-centered solicitude of the child based on its own physical discomforts. Hence one finds the expression of behavior in terms of compulsions, anxieties and undue fixation on intestinal activity. The physiologic factors are somewhat more in the forefront of the child's thinking, although the social element has had a definite place in magnifying its importance.

The fourth group differs from the first in that the parental attitude has not set up a series of biologic social threats, and the child has accepted its socially deviating bowel rhythm as physiologically normal. In this type, adjustments of dietary and minimization of the necessity of routine stools are the outstanding items. There is, however, a consciousness of social variations without abnormal reactions.

The behavior which results from each of these various types is obvious. It is not possible, of course, to differentiate entirely the symptoms which arise from the sluggish bowels, per se, but there are some seemingly definite behavior types which grow out of each of these forms by reason of the underlying psychologic relations of the personal physiologic fact to the norm of social intestinal habit.

I shall discuss practically only the second and third groups as manifest in half a dozen typical case histories. Sharp differentiation between solicitude of the parent and solicitude of the child is not always possible. Occasionally the solicitude of the child is primary, although in the large majority of cases it is a secondary phenomenon induced by the parental solicitude. The separation of the influences affecting these types can be secured only by attention to the primary factors entering into behavior. An infant, constipated by reason of a concentrated milk diet, may suffer severe pain as a result of an effort to evacuate a large, hard, dry stool, and from this event there may develop a fear of evacuation which in itself conduces to constipation because pain inhibits peristalsis. This would represent an origin specifically in the physical reaction of the child. If, however, the child has no difficulty with his stools, but the parent begins early to use enemas and drugs for the purpose of securing daily movements of the bowels, the child gains a sense of importance of this phenomenon by reason of rectal manipulation. The primary cause of such self-centeredness in evacuation is inherent in the

parental solicitude. Both types may be further modified when the child's age enables him to appreciate the verbal comments of the parents on why there should be daily evacuations and what symptoms may arise if the bowels fail to perform thus regularly. The acceptance of the parental ideation too frequently serves as the groundwork for building up a symptomatology which tends toward introversion and profoundly affects mental attitudes regarding personal behavior. Further ideas concerning the principles entering into defecation and the inculcation of ideas of modesty, shame and other taboo reactions regarding this act develop a new series of phenomena which have definite influence on social behavior.

The group of children whom I have selected as the basis of discussion are to be regarded as manifesting psychic constipation because physiologically their bowels would move with a definite rhythm if not hampered by interference. Their constipation was induced by the routine attention to their intestinal tracts, and their behavior reactions are incidental to the manipulations and attention rather than to an essential constipation. The main symptoms manifested by the group include anorexia, restlessness, irritability, crying, exhibitions of dependence and at times tics, temper tantrums, headaches and a tendency to keep away from other children. This group of symptoms is not specific for constipation, but may exist with a variety of causes, just as do other symptoms found in my group, such as talking in the sleep, masturbation and mucous colitis. The significant relation between constipation and these various symptoms, any one of which may constitute a problem, lies in the fact that they have disappeared with the therapeutic attack made directly on the constipation factor. And the main therapeusis has been reeducation of the parents and children, the cessation of administration of drugs and enemas and reassurance as to the safety of natural physiologic intestinal rhythm following a balanced dietary.

The ages at which the children were first seen were, respectively, 4 years and 10 months, 5 years and 5 months, 7 years, 8 years and 1 months, 12 years and 3 months and 13 years. The entire group was asthenic in type. In height, these children showed a tendency to be below the standard average for age. A boy aged 12 years and 3 months was 7 inches (17.7 cm.) above the average height, while the boy, aged 13 years, was 11 inches (27.9 cm.) below the average. The girl, aged 4 years and 10 months, was 5 inches (12.7 cm.) below the theoretical average height, while a girl aged 5 years and 5 months was 3½ inches (8.8 cm.) above the average height for her age. One cannot place too much stress on this variation in height without a consideration of the family stock. It is significant, however, that the general trend was found to be below the norm for the age and sex.

The weight was entirely uniform in the group. All the children in this category were below the average weight for their age and height.

This, of course, becomes more significant in view of the fact that the constipation was accompanied by pronounced anorexia and finicky attitudes toward food. The accompanying table indicates the degree of underweight for age and height in this group. The marked degree of underweight of the two adolescent children is noteworthy.

The general intelligence levels of the group are adequate, the intelligence quotient varying from 87 to 121, with the median at 94. No definite changes were noted as a result of treatment or change in the bowel movement cycle..

For those who see a hereditary picture in constipation, it is interesting to note that in the heredity of this group of six, any and all possibly significant factors are in the maternal line. The fact that constipation is more common among females probably holds no relationship to the nervous conditions existent in the maternal family life.

Age	Amount Below Theoretical Weight, Pounds
4 years and 10 months	3½
5 years and 5 months	2
7 years	2½
8 years and 1 month	3
12 years and 3 months	8
13 years	17

Of the heredity in the six families, the following comments may be made:

Case 1.—One maternal aunt with epilepsy and one cousin, a child of another maternal aunt, epileptic.

Case 2.—Maternal grandmother, possibly feebleminded; maternal aunt, epileptic fugue states; mother, mild manic-depressive psychosis.

Case 3.—Maternal cousin insane; mother and two maternal aunts, frequent headaches.

Case 4.—One maternal uncle possibly psychoneurotic; mother, cardiac neurosis.

Case 5.—Mother hypochondrical.

Case 6.—No evidence of nervous and mental disorders.

The ages of the parents in this group of children are significant only to the extent that they help explain unusual interest and solicitude for the children. The parents of three of the children were middle aged, and the parents of the other three were in the thirties.

The position of the child in the family is suggestive of some significance in relation to social pressures.

Case 1.—This child was the youngest of four, but with four years between her and the next older child, thus giving her somewhat the situation of an only child.

Case 2.—This child was the older of two, with four years between their births.

CASE 3.—In this case the patient was an only child.

CASE 4.—This case concerns an only child, but one who had been preceded by an infant who died at birth.

CASE 5.—The child was the oldest of three children, with only a year and a half between himself and the succeeding child.

CASE 6.—This was the older of two children, with a birth interval of two years.

This is too small a group to justify any statement concerning the position of the child in the family. It is suggestive, however, that the fact that the patient is an only child is a factor in determining some of the symptomatology which exists in this group of constipated children.

Still more important, however, are the general social conditioning attitudes of the mothers. These may again be tabulated in order:

CASE 1.—The mother had always worried about her sister's epileptic attacks, and she has never told anyone, not even her husband, of these attacks. The patient had been to several hospitals. The mother was overanxious about the child's condition.

CASE 2.—The mother and father quarreled because of a lack of marital sexual adjustment; the mother admitted her responsibility and regarded the child as the object of greatest solicitude.

CASE 3.—The parents were middle-aged and fussed over the child continually. The home life was not too congenial by reason of the mother's resentment of the husband's economic inadequacy. There was much talk in the home concerning the ill health of the boy and his mother. In this family the first child was born dead, and the second child, now an only child, received extra solicitude.

CASE 4.—The mother had a cardiac neurosis; she was hypochondriacal about herself and extended the anxieties to her child; she talked continually about her own state to the child and about its own symptoms.

CASE 5.—The mother was oversolicitous with reference to the patient, particularly by reason of his complaint of pain and headaches.

CASE 6.—The mother had been exceedingly nervous over the boy's condition ever since he had an attack of mucous colitis. The parents worried about financial reverses which they endeavored to hide from their children. The whole family revolved about the patient's condition.

It is obvious that attitudes of this kind with reference to the child may be confused with some of the elements that I have referred to in connection with heredity, but the attitudes are based in a large measure on a belief in the necessity for daily evacuation of the bowels. In every instance physics had been given, enemas had been employed and various drugs had been utilized over long periods of time. In order to give a picture of these specific children I am going to present in abstract form their problems and development, stressing elements that are significant. To illustrate the progress of the cases, I shall present a brief description, based on clinical notes, of their behavior and its relation to the state of constipation from the time the child came under observation until the middle of January, 1929. I shall omit items that are not germane to the central theme.

REPORT OF CASES

CASE 1.—*A girl, first seen, September, 1928. Problem as presented: Poor appetite, restless sleep, attacks of twitching of the face and body, constipation; seldom had a natural bowel movement; physics used daily. The twitching of the face occurred two or three times a day.*

The pregnancy, birth, and early development had been normal. Infantile dependence was now present, and the parents were lenient with the child because of her physical condition. The girl played well with children and got on well with her brothers and sisters, who treated her like a baby. She had whooping cough at 1 year of age, chickenpox at 2 years and diphtheria at 3 years; some caries of the teeth and a palpable thyroid gland were present. She was not in school..

At the first visitation, all stress on feeding was removed; there was some suggestion regarding general dietary, and the use of a cathartic was interdicted. The following week the mother reported that no cathartics had been used and that the behavior had been somewhat better. The original twitchings were now reported as being attacks of "body quivers"; the child had a feeling of falling when the spell came and cried for the mother. The child had some attacks when 17 months of age and occasionally had two or three a day. The neurologic report stated, "These seizures in association with history of mental and physical retardation and few organic neurologic findings indicate organic epilepsy." Observation in the hospital had been advised, but the advice had not yet been accepted. The epileptiform seizures had no evident relation to the constipation.

On October 17, practically a month after the child had been seen first, the mother reported that the child played better since she had been coming to the clinic and that she ate better. She had gained 1 pound (0.5 Kg.) during the month. In December, the mother reported that the child was sleeping better, still gaining in weight, that no more cathartics were employed and no further attention was given to the constipation, as stools occurred at fairly regular intervals. The attacks still occurred, and apparently the epilepsy in the mother's family was becoming more evident in the child.

CASE 2.—*A girl, aged 5 years and 5 months. Problem: Child cried, was restless, had temper tantrums and talked in sleep. Refused to eat, did not play with children and was constipated.*

The pregnancy and birth were normal. The early development of the child was normal. The past medical history showed: measles at 3 years; the tonsils and adenoids removed; frequent cough, poor appetite and constipation always present. The physical examination revealed palpable anterior and posterior cervical glands, a high arched palate, scoliosis, pronation of the feet, genu valgum, a functional systolic murmur at the base of the heart; the liver 1 fingerbreadth below the costal margin; diastasis of the rectus muscles; webbing of the third and fourth toes. Although this child had an intelligence quotient of 121 she was not attending school. She responded to attention and evidenced no special shyness but a large degree of quarrelsomeness.

When the child was first seen on July 22, 1927, because of the mother's neurotic condition and the friction between the mother and the child, outside placement was suggested. The mother was a sadistic, mild manic type. She would not let the child go to kindergarten at times because she would not eat breakfast. Cathartics again were interdicted, and the maternal emphasis on food was lessened. In the middle of September, the mother reported improvement in the general behavior. The mother did not bring the child in for eight months, and again was advised to place the child outside of the home, particularly as there was a recurrence of the

difficulties in social adjustment with the parents. This advice was not followed, and three months later, in November, the mother reported that the child was much better, was getting along well in school, and that no further attention was being paid to the constipation; all cathartics had been discontinued and the bowel movements had become fairly regular.

When she was first seen by me one could not determine the cycle of bowel movement because a cathartic was given so regularly that the bowels never had a chance to move naturally. In this instance, while there was adjustment in school and the general behavior had improved, together with the condition of the bowels, the situation in the home remained a matter for further attention.

CASE 3.—*A boy, aged 7 years. Problem: Restlessness and chronic constipation. Had vomiting spells every three or four months for four days; bowels never moved without medicine; daily enema; child always on some kind of a diet; played little with boys and would stay at nothing very long.*

The mother had headaches during pregnancy, but the child's birth was normal. The past medical history was unimportant, except for measles and the restlessness in sleeping, vomiting spells and anorexia. The physical examination showed some enlarged glands of the neck, open mouth, nail biting and facial asymmetry. The intelligence quotient was 92. The boy apparently had no idea how to play and had ill health most of the time.

He was first seen in April, 1926. The boy's bowels had been moved artificially every day, practically, since birth. He had never had any constant laxative diet because he did not like to eat, particularly the kinds of food that had been advised. The attitude of the mother toward the child was constantly negative—"he will not eat," "his bowels will not move," "he will not play," etc. The boy always played with younger children. The mother was afraid he might get hurt with older children. The child was wont to complain of cramps and pains in the abdomen.

It was necessary to educate the parents as well as the child. During the first three weeks, the parents permitted the child to go from Wednesday to Saturday and from Saturday to Monday before giving an enema. A special dietary was given of food with considerable residue.

A report from the x-ray department indicated that the gastro-intestinal canal gave no evidence of an organic lesion. "The stomach was situated normally; the gastric tone, peristalsis and motility were normal; no abnormality was noted in the duodenal bulb; six hours after food was taken, the stomach was empty; at this time some of the barium was in the small intestine and the rest in the colon to the distal third of the transverse portion. Twenty-four hours after food was taken, the colon was empty with the exception of a large bolus in the rectum. This is evidently a case of obstipation."

During the following month, there was an attack of pavor nocturnus. The mother refused to allow hospitalization. Mineral oil was tried as a substitute for cathartics, and the mother permitted the child to go again for three days without bowel movements. In July, the boy complained of cramps, but two months later, during which time mineral oil was used, it was reported that the constipation had diminished and that he was not being given enemas. The mother stated that she was afraid to allow him to play in the street because she could not watch him. Other children did not like him. The child had no idea of how to play with other children.

During the five months there had been no increase in weight, but a definite improvement in the condition of the bowels. He entered school and began to make slow but natural adjustments to the school work. His behavior began to

change again, and he was calling his parents "bad names," while the mother was hitting him daily to make him go to school. The father was afraid he would not be promoted and was having difficulty with the school. As a result of his interference, the boy was transferred into an ungraded class. The reason for the father's difficulty with the school authorities lay in the fact that the toilet for the class was in the back yard; he feared the effect of this on the child and wished him transferred into a class where he could use an indoor toilet. The result of the situation at school was a pronounced maladjustment which took considerable time to straighten out.

In the meantime, the boy had overcome his sensitiveness to abdominal pain, of which he had earlier complained; he had had no cramps, and during a period of eight months, up to March, 1926, he had gained 6 pounds (2.7 Kg.). During the summer of 1926, the boy was sent away to the country, and his parents were permitted at times to visit him. There was marked nostalgia, but the parents agreed to permit him to remain. During the summer at camp the condition of the bowels improved, and no medicine was being employed unless the bowels did not move during the entire week.

In October, 1926, the mother's attitude changed somewhat, and she was willing to allow the boy to dress and bathe himself. His bowel movements became poor again after his return home. His behavior reverted again to the type that was more common in the home than at camp. The mother began again to give him mineral oil because of the irregularity of the stools. In November, 1926, he was having stools once in four days, but no enemas were being employed; no improvement in his school work was reported; during the next month he did not receive medicine for more than three weeks, and did not complain of pain while his bowels were moving of their own accord, but at intervals of several days.

By the end of March, 1927, his weight had increased 21 pounds (9.5 Kg.), in two years, or to 72½ pounds (32.9 Kg.); his school reports indicated better work; he was removed from the ungraded class. The mother was still dressing the child, taking him out, going to school to take his part whenever there was any difficulty with other children, and there was general protection of the child in every way.

By the end of June, 1928, he had passed into the fourth grade with a good record in conduct and was fairly well adjusted with other children. His attendance at school was regular, and he manifested no neurotic symptoms or unpleasant behavior at the school. The mother stated at this time that recently there had been some vomiting every four or five days and headaches about three times a week, with regular bowel movements every three or four days. The evidence of the mother fixation was seen in his crying for his mother to come to his room and lie on a nearby bed until he slept. This had been continued for a period of years. His diet was inadequate and vegetables insufficient. He was again sent away for July and August, and the authorities at the summer camp reported that he vomited every time his parents visited him and at no other time. In October, 1928, the boy weighed 91 pounds (41.3 Kg.) and was still doing well at school; during some periods his bowels moved every day and during other periods, every other day. No further attention was paid to the constipation; he was not receiving any enemas or cathartics, and there was no vomiting; his adjustment in school was adequate and his social relationships were satisfactory. It was still necessary to hold his middle-aged parents to an appreciation of the value of noninterference and to give the patient a larger opportunity to play with children of all kinds under more normal conditions.

CASE 4.—*A girl, aged 8 years and 1 month. Problem: Did not eat; was fussy about food; cried a great deal; talked in her sleep; had tics of the eyes and mouth; had practiced some masturbation for the past two years; had chronic constipation.*

The child weighed 4½ pounds (2.04 Gm.) at birth, which was normal; feeding was difficult during infancy, so much so that the mother remarked, "I always thought she would die." She had had occasional attacks of vomiting since infancy. She had had measles, whooping cough and chickenpox; the tonsils and adenoids had been removed. Physical examination revealed palpable anterior and posterior cervical glands, a high, arched palate, deviated nasal septum, ptosis of the right eye, scoliosis and fecal masses palpable over the entire ascending and descending colon.

The intelligence quotient was 94. The child was somewhat unresponsive.

She was first seen in September, 1927. On examination, the blood showed a slight secondary anemia. A roentgenogram of the legs showed a suggestion of a localized inflammatory lesion of one of the tibia with a small punched out area in the lower end of the diaphysis. There was slight facial paralysis, and the thyroid gland was somewhat enlarged.

The general dietary was defective in proteins, and the regular use of laxatives directed too much attention to constipation. A change in dietary was instituted and drugs stopped. A month later it was reported that the child was still crying and talking in her sleep and eating inadequately, although the tics of the eyes were somewhat better. The weight was stationary. There was an interval of digestive disturbance, and the project of eating more concentrated foods with vegetables was presented to the child, who accepted it.

In December, at the end of three months, the mother reported definite improvement in the child's reactions, an improvement in eating with more natural stools, diminished tics and a 2 pound gain in weight. In March, the child began to complain of dreams concerning her ears, which apparently referred to the year previous when an operation on the ear had been suggested but was not regarded as necessary; recently, she had had earaches. In April, she was told that she had something wrong with her heart by a school nurse, although physical examination did not disclose this. The child no longer complained about abdominal pains. She began to be interested in her foods and started to eat bananas daily in June, 1928. By November, 1928, during a period of five months, she had gained 5½ pounds (2.5 Kg.), and her bowels moved regularly every two or three days without the use of a physic. She had eaten a larger variety of vegetables than ever before; the tics had entirely disappeared; there had been no further talking in her sleep; masturbation had ceased entirely. At present, the regular cycle of bowel movement was every two or three days, but it is possible that with a larger amount of vegetables this cycle may be altered. During the year and a fourth, therefore, she gained more than 7 pounds (3.2 Kg.) and there was cessation of practically all the symptoms originally complained of without specific attention to any factor except the intestinal ailment.

CASE 5.—*A boy, aged 12 years and 3 months. Problem: Severe pains in the head and eyes; always a pain somewhere. Chronically constipated; mother gave enemas daily; the child spoke of pain over his heart and located the pain over the umbilicus.*

The first headaches began after the boy had failed to be promoted in school two years previously. It is significant that his headaches were never severe enough to interfere with his playing. He cried with pain frequently just before going to bed; he said that his eyes burned and that then the pain went through his head. He remarked, "I have wheels in my head."

The delivery was normal at full term. Every development was thoroughly normal. Sleep was restless and was accompanied by dreams relating to fire and other anxiety interests. The daily dietary was comparatively free from vegetables and fats and consisted mainly of milk in some form and some carbohydrates. The child was an intraverted type without outside interests and had difficulty in making friends. He whined to secure his purpose. He did not play well with other children. There was no marked diversity of intellectual interest; school was possibly somewhat difficult for him, and the headaches might be part of an escape mechanism. The intelligence quotient was 87, with a mental age of 10 years and 10 months and a school placement in the 6-A grade, which was an acceleration over his mental age. His actual achievements in arithmetic were below the expectations for his mental age.

He had had measles and an operation for hernia. There was nothing unusual in his physical makeup except his general asthenic build.

This boy had been in the hospital, and his headaches were regarded as possibly being migraine. His eyes had been examined and glasses supplied without relief. He was constantly referring to pain in one part of the body or another. On examination, however, these abdominal pains were not present if he were distracted by conversation. Attention to the diet was immediately given, and the family was directed to discontinue the enemas. Within three months, his weight increased 7 pounds (3.1 Kg.).

He was sent away to camp for the summer, and the authorities at camp reported that the boy complained of various aches and pains and that his bowels had not moved for two weeks so far as was known. On his return home the mother again began to resort to enemas, but only about once a week when he complained occasionally of pains in the stomach. The boy stated that "Mother does not know how to prepare proper food for me," and a more detailed teaching of dietetic methods was undertaken. By December, ten months from the time he was first seen, his weight had risen to 95 pounds (43.1 Kg.), a gain of 17 pounds (7.7 Kg.), which represented the amount that he was underweight..

The boy stated that he would be well if he did not have to take an enema. His mother no longer gave them to him, but he took one sometimes every second day. He was asked to stop the enemas entirely, and his bowels began to act regularly, though at times only every third or fourth day. It is significant that the pains formerly attributed to the constipation continued to be present only in the morning before he went to school and only on school days. He was having some difficulty with arithmetic and was incapable of doing the work. A tutor was to be secured.

The last report indicated that the bowels were moving without enemas or cathartics; that his headaches no longer existed; nor were there complaints about his eyes. He was doing as well as could be expected in school with his dulness.

CASE 6.—*A boy, aged 13 years. Problem: Chronic constipation.*

It was stated that nine months before, after visiting his aunt's home where he was to spend the summer, the boy had an attack of mucous colitis. He had never been separated from his mother before. Though he returned home immediately, he had had a poor appetite ever since and had not had any natural bowel movements for five months. He read medical books and thought that he had symptoms of a large variety of diseases concerning which he had read. He had been under observation at the hospital and the notes at discharge included the following: "While here gained 3 pounds, felt well; x-ray and other examinations did not reveal any pathologic condition; patient discharged, improved. Diagnosis: chronic constipation and chronic appendicitis."

The early development was normal; he had had whooping cough, chickenpox, pneumonia and colitis. There was irregular dentition, with high arched palate, some facial asymmetry due to the irregular dentition, sallowness, marked anemia, slight enlargement of the liver and a palpable thyroid.

The boy had not been in school for four months. His intelligence quotient was 117, and he had been doing thoroughly adequate work in school. He had been getting along well with boys but had difficulty with rough boys. He enjoyed adult companionship and helped around the house. He was sensitive, wished to attend school and prayed to be like other boys who went to school. He lacked confidence in himself and was inadequate in his relationship with other children in the street.

He was first seen on March 10, 1926, after the mother reported that he had been ill all night. Another roentgenogram of the gastro-intestinal tract revealed a gastrocoloptosis and extremely delayed motility of the colon; no other abnormalities were noted. Cathartics and enemas were interdicted. In one month he gained approximately 2 pounds (0.9 Kg.). There were occasional abdominal pains, at times during the day and at other times during the night. He had gone as long as twelve days without an evacuation. He was advised to return to school. He attended school one day, and then it was reported that he had become ill and remained away. He complained of pains, but examination a few days later showed no distention of the abdomen or pain. The boy tried again to go to school. The following months it was learned that he was not at school regularly and he was given mineral oil, as a result of which he had natural stools at two, four and five day intervals. There were occasions, however, when the mother insisted on the use of suppositories. It was insisted that the boy go to school regularly.

In the beginning of the summer, about five weeks later, it was learned that for several weeks he had had no natural movement because he had used suppositories again. The biology and hygiene of the intestinal tract and defecation were explained more fully to the boy, and a laxative diet was elaborated, which consisted of plenty of green vegetables, raw fruits, plenty of water, etc. Suppositories were no longer to be used.

Two months later, the mother reported that the boy had improved very much and was starting to school at the beginning of the year. He had natural bowel movements on Monday and Thursday of each week. During the six months' interval he had gained 17 pounds (7.7 Kg.). He was no longer taking any medicine, and there were some days when he had four or five stools daily; this was probably due to an irritative diarrhea caused by dry, irritating fecal masses. It was now reported that the boy was still interested in his physical condition. After the death of Valentino, he became more specifically interested in his own condition and became fearful of peritonitis and therefore did not want to neglect his bowels. The mother was busy questioning him in regard to his pains and discussing every symptom with him. It was suggested that the boy go away from home to a winter camp, whereupon both the mother and the boy evidenced marked distress, and the boy was almost fearful of the examiner.

An examination of the feces at this time revealed nothing pathologic.

Four months later the mother reported that the patient was continuously improving with, however, another temporary setback in attitude in regard to his bowels when he heard of the death of some notable after appendectomy The boy actually got his mother to call in a physician to convince him that his appendix was undiseased.

A later record indicated a complete improvement in the condition without dependence on any outside aids for evacuation and that he had not seen any more physicians. A report a year later, in November, 1928, indicated that the boy

was in an excellent condition and weighed 127 pounds (57.6 Kg.), which represented an increase of 62 pounds (8.1 Kg.) in two and a half years. He was interested in athletics, had joined various clubs, was doing excellent work in the fifth term of high school, and his bowels moved regularly every third day. There was no longer any complaint of pain or distress. Neither the boy nor the mother was further worried about his bowels, but there were still rare occasions when a suppository was used.

COMMENT

This series of children with constipation indicates that the behavior reactions incidental to constipation belong definitely to two categories already mentioned. First come the reactions essentially due to the biologic manifestations of intestinal torpidity, sluggishness and the like, involving a sense of discomfort, fulness in the abdomen, a feeling of distention, flatulence, borborygmus, occasional pains, loss of appetite and possibly irritability, fatigability, and diminished attentiveness or even restlessness due to toxic absorption.

The second group of behavior reactions involve responses to social elements bound up in prevailing ideas concerning the necessity for routine daily evacuations of the bowels and the general social acceptance of the importance of regular daily stools for the perfection of health and welfare. The widespread belief that many minor ailments and general diseases arise from constipation leads to the centering of considerable parental solicitude on intestinal activity. The social factors are productive of fears, anxieties and certain compulsive elements which enter into behavior. The social pressures appear to encourage introverted trends.

A third set of behavior reactions results from the employment of various means to bring about the adaptation of the child's bowels to the principles of activity socially believed to condition his health.

The details of the effect of the employment of special drugs, mechanical devices and manipulation of the anus and rectum are unnecessary because they are not generic but specific for individual children.

In the behavior of a single child, a number of these elements may be marked. A child with a slight fissure in ano which caused severe pain hesitated to defecate, resisted the call and became constipated. The mother, unaware of the difficulty, gave a cathartic which increased the necessity for evacuations and heightened the pain, which in turn intensified the fear of the child with reference to stools. The use of the cathartic similarly brought about a tendency to a compensatory constipation, as a secondary reaction. The increasing constipation brought about a larger concentration of maternal efforts to make the bowels move. The child was queried repeatedly concerning whether his bowels had moved, how much and what kind of stools he passed and whether it was necessary for the mother to give more or less medicine, use a suppository, give an enema or an irrigation. The child came to recognize

in his bowel movements an important part of his being, and his intestinal activity became a part of his routine conscious life as related to his parents.

The parental stress placed on stools, together with the actual constipation and his own painful reactions thereto, led to a decrease of appetite, a heightening of his irritability, the development of a sensitivity and a building up of a still greater guarding of his health by his parents. The fears for him increased, and their protection even extended to his companionships. Gradually he was given less opportunity to play with other children, and he was cautioned against rough boys and in turn he began to shun normal companionships and play. Repeatedly he was questioned whether his eyes hurt, or if he had headaches. The association between constipation and headaches was readily made by him, and the headache became an instrument for his own defense against undesirable demands made on him. The headache became an instrument to escape school, to refuse errands and to avoid the ordinary difficulties of life. The basic constipation was still being attacked by the use of enemas, suppositories or cathartics, even though the fissure had long been healed. There was inherent in his behavior all of the elements which had arisen from the original pain, the original maternal solicitude for daily movements and the original use of materials to induce defecation.

With the cessation of all external means of stimulation of the bowels, after due reassurance of parents and patient, the various types of behavior previously mentioned slowly departed without specific attention having been given to any one of them. His normal bowel cycle was a movement every third or fourth day and, once this was achieved, he proceeded to live in harmony with this physiologic rhythm. His constipation no longer was the center of his introverting life, his thinking and his actions. He became more extravert and gradually assumed normal social relationships.

It is important to call attention to the part that constipation may play in the behavior of children, not because it is such a significant factor, but because frequently attention to this single symptom may free the patient from a variety of fears and asocial behavior trends.

Constipation has comparatively little specific effect on intellectual activity and only a slight effect on physical vigor. The attitudes toward the bowels, however, and the social implications of costiveness are far more important. A constipated child may present problems in behavior which may be equally common among nonconstipated children. The opportunity to relieve the specific behavior giving rise to complaint lies in a recognition of the fact that constipation may be a dominant factor in causation. The recognition of the biologic and social phases of intestinal action assists in securing a more favorable solution of the problem of behavior conditioned by reactions to a constipation that is the central factor in a total situation.

Pediatric Biographies

JOHN MAYOW
1643-1679

JOHN RUHRÄH, M.D.
BALTIMORE

This neglected genius, who had one of the most brilliant intellects of the seventeenth century, may be included in the list of those who helped in the growth of pediatric knowledge chiefly on account of his contributions on rickets. His family was an old one, living at Bree, in Cornwall, but he himself was born in the Parish of St. Dunstan in the West, in Fleet Street, London, in May, 1643. At the age of 16 he was received as a commoner at Wadham College, Oxford, and admitted as a scholar on Sept. 23, 1659. He was later elected to a fellowship in All Soul's College and was graduated Bachelor of Civil Law in 1665, and D. C. L. in 1670. He was given the privilege of studying physic, which exempted him from taking holy orders. He went to London, but was never elected to the College of Physicians. He practiced at Bath, especially in the summertime, where his reputation was great, but, as Wood quaintly stated, he was "better known by these books which shew the pregnancy of his parts." He died in London in 1678, and was buried in St. Pauls, Covent Garden, as had been Richard Wiseman two years before.

Mayow's work was chiefly concerned with chemistry and physiology, and his contributions so long neglected long after his death began to attract attention, until now he is recognized as one of the great lights of English science.

One of the most delightful accounts is by Gotch, the Waynplete Professor of Physiology at Oxford, entitled "Two Oxford Physiologists", in which there is an excellent description of the philosopher's attitude toward the phenomena of life. Mayow's "De Sal-Nitro" led to his election to the Royal Society. His first work, "De Respiratione" appeared in 1668, and was followed in 1673 by "De Rachitide"; these were republished at Oxford together with three other tracts with the following title page:

> Tractatus quinque medico-physici.
> Quorum primis agit de
> sal-nitro et spiritu nitro-aero.
> Secundus de respiratione.
> Tertius de respiratione foetus
> in utero et oro. Quartus
> de moto musculari et spiritibus animalibus
> Ultimus de rachitide.
> Studio *Joh. Mayow*, LLD. et Medici
> Necnon Coll. omn. anim. in
> Univ. Oxon. Socii.
> Oxonii E Theati Sheldoniano,
> An Dom. MDCLXXIV.

This work was republished at The Hague in 1681 under the title of "Opera Omnia", and at Geneva in 1685. Translations were made into Dutch (1684), German (1799) and French (1840). This "Tractatus Quinque" is one of the great masterpieces of science. Mayow contributed to anatomy, to chemistry, to physiology and to clinical medicine. He described the double articulation of the ribs and the spine and the action of the intercostal muscles; his experiments dealt with the processes involved in rust, in fermentation and in combustion. He demonstrated the nature of combustion a hundred years before Lavoisier. His ideas were the same, though naturally his terminology was different. He showed the part played by the placenta in supplying the aerial part necessary to life. These are but a few of his many contributions. His early death cut short one of the most promising scientific careers of his age.

TRACTATUS SECUNDUS,

DE

RACHITIDE.

A

JOH: MAYOW, *Oxon. Coll:*

Omn: An: Socio.

Title page of John Mayow's book on rickets.

The little book on rickets, which was also reprinted separately, is in the Army Medical Library. It is interesting to compare his style with that of Glisson. Mayow gives but a skeleton of facts, omitting all discussion. One extract will serve as an example:

OF THE SIGNS OR SYMPTOMS OF THE DISEASE

The Diagnosis or knowledge of the Disease, (as of others,) doth depend upon the understanding of the Symptoms, which are these that follow.

1. The proportion of the parts if irregular: *viz.* The *Head* bigger than it ought to be.
2. The *Face* over-fat.
3. The *Wit* too acute in respect of the Age.
4. The external *Members,* chiefly the musculous, lean and extenuated.
5. The *Skin* loose and slagging.
6. The *Bones* for the most part bowed, and those about The Joynts standing out, and knotty.
7. The *Spine* or Back-bone is variously inflected.
8. The *Breast* is straight or narrow.
9. The Extremities of the *Ribs* knotty.

10. The *Abdomen* somewhat puffed up, and stretched out. These things are outwardly observed, but inwardly.

11. The *Liver* is perceived over-large; as also most of the *Parenchymaes,* or fleshy substances.

12. The *Ventricle* and *Intestines* rise into a greater Bulk, than in those who are sound.

13. The *Mesenterium* is affected with Glandules too great; if not with *Strumae* or Waddles.

These are the Symptoms within the *Abdomen;* with the breast,

14. The *Lungs* are discerned stuft and tumid; and the same sometimes purulent, strumous, and very often growing fast to the *Pleura.*

15. The *Jugular Veins,* and *Carotid Arteries,* are sometimes found larger than their just proportion; but the Brain is faulty only as to its Proportion and massy Bulk.

16. Lastly, to these is added an *Enervation* of almost all the parts; also a certain drowsiness and Impatience of Labour and Exercise: For, the little Children cannot play, except sitting, and with much ado can stand on their feet. And at last in the Progress of the Disease, the burthen of their Head, can hardly be sustained by their weak neck.

These are the so many and so great Symptoms of this Malady: In the next place we must search out what may be the fruitful cause or michief of so numerous an off-spring.

Another interesting bit concerns the use of hyperemia, as recently suggested by Bier for various joint disorders. This also occurs in Glisson.

Moreover, *Ligatures* fitted to the Thigh and Leg upon the Knee, and to the Arms upon the Elbow avail much; but they must be loose enough and soft, so as they may not hinder the increment or thriving of the Part whereunto they are applied: For the Utility of Ligatures consisteth in this; that they help to revel the afflux of Blood from the Head, & to deduce it towards the extenuated Parts. To this Title may be refer'd *Fasciatio,* or the Swathing of certain parts; as likewise *button'd Boots,* wch help much not only to strengthen the Parts, but further to correct the Crookedness of the Bones, and bending of the Joynts. But in the use of these, care must be taken, that they press down a little the protuberant part of the Bone, but hardly touch the hollow part.

News and Comment

GENERAL

President Hoover Calls Conference on Child Health.—It was announced, July 2, that President Hoover had decided to call a White House conference on the health and protection of children. The members will comprise representatives of the great voluntary associations and federal, state and municipal authorities interested. The conference will not be assembled for nine months or a year, but the first meeting of the planning committee was held in Washington, July 29. The President announced that a series of committees will be appointed from the leaders in national organizations. The purpose will be to determine the facts as to the present progress and future needs in this field and to make such recommendations for measures for more effective official and voluntary action and their coordination as will further develop care and protection of children. The subjects to be studied embrace regular medical examinations, school or public clinics for children, hospitalization, adequate milk supplies, community nurses, maternity instruction and nurses, teaching of health in the schools, facilities for playgrounds and recreation, dependent children, voluntary organization of children, child labor and scores of allied subjects. A sum of $500,000 from private sources has been placed at the disposal of the President to cover the expenses of the preliminary committees, and the conference, and the follow-up work which will be required to carry out its conclusions. The work of the conference will be under the direction of the secretary of the interior, Dr. Ray Lyman Wilbur, with the cooperation of the secretary of labor, James J. Davis. The executive secretary will be Harry E. Barnard, Ph.D., a chemist, and former director of the American Institute of Baking, Chicago; former secretary of the American Bakers' Association; president of the Lake Michigan Water Commission; state food and drug commissioner of Indiana; state commissioner of weights and measures of Indiana; food and drug inspection chemist of the U. S. Department of Agriculture; president of the Indiana Water Supply Association; a director of the American Chemical Society, and federal food administrator for Indiana. Dr. Barnard left the American Institute of Baking in 1928 to become head of the American Honey Institute in Indianapolis, which was formed following a meeting of the Bee Industries Association of America in that year (THE JOURNAL, June 9, 1928, p. 1877). The planning committee present at this meeting was comprised of: Dr. Ray Lyman Wilbur, chairman, secretary of the interior; Edgar Rickard, mining engineer, assistant to President Hoover when he was U. S. food administrator, treasurer, New York; Harry E. Barnard, Ph.D., executive secretary, Indianapolis; Grace Abbott, children's bureau, U. S. Department of Labor; Henry Breckinridge, National Amateur Athletic Federation, New York; Mrs. Grace S. Burlingham, St. Louis; Bailey B. Burritt, Association for Improving the Condition of the Poor, New York; Judge Frederick P. Cabot, Boston; Frank Cody, superintendent of schools of Detroit; Dr. S. J. Crumbine, American Child Health Association, New York; Dr. Hugh S. Cumming, surgeon general, U. S. Public Health Service; Lee K. Frankel, Ph.D., Metropolitan Life Insurance Company, New York; William M. Green, president, American Federation of Labor; Gertrude B. Lane, editor of the *Woman's Home Companion*, New York; Mrs. William Brown Meloney, New York *Herald Tribune*, New York; Mrs. Elizabeth A. Perkins, department of child welfare, World's W. C. T. U., Evanston; Mrs. Raymond Robins, social economist, Brooksville, Fla.; Mrs. F. Louis Slade, New York; Dr. William F. Snow, National Health Council, New York; Louise Stanley, Ph.D., bureau of home economics, department of agriculture; French Strother, former congressman from Virginia, White House; Samuel M. Hamill, past president, American Pediatric Society, Philadelphia; Dr. William F. King, state health commissioner of Indiana.

In addressing the planning committee, President Hoover is reported to have said:

"Through Secretary Wilbur and Secretary Davis I have invited you here as the nuclei of a planning committee to inaugurate a movement most important to the nation as a whole. That is, that we should take national stock of the progress and present situation in the health and protection of childhood; that out of this investigation we should also develop common sense plans for the further advancement in these directions. I have suggested that in order that these investigations and recommendations may be brought about in the most effective manner, a number of committees should be organized to cover different phases of the subject, embracing the leadership in thought and knowledge of these subjects throughout the nation; that after these investigations have been carried forward and conclusions reached by these committees, we should call a White House conference of public officials, associations and others interested in these questions, to consider the recommendations. Further, that such of the policies that may be adopted by that conference should be followed up by definite organization throughout the country. We realize that major progress in this direction must be made by voluntary action and by activities of local government. The federal government has some important functions to perform in these particulars, all of which will need to be considered, but we may save years in national progress if we can secure some measure of unity as to view and unity as to program, more especially as these views and programs are to be based on searching examination of fact and experience. Generous means have been provided to enable you to carry forward this task without difficulty, and I wish to assure you of the complete support of the executive."

It is suprising that President Hoover has not shown more recognition of any organized medical group in his choices. While there are a few medical men on the board, neither the American Medical Association nor the American Pediatric Society has been asked for its cooperation.

Child Hygiene Institute at Winona Lake, Ind.—The State Board of Health of Indiana conducted its annual child hygiene institute at Winona Lake, Ind., July 15 to 19. The program included motion pictures, models and demonstrations. One hundred and forty-one babies and children of preschool age were examined, and 2,500 people saw the health films.

UNIVERSITY NEWS

Dr. R. M. Smith Receives Honorary Degree.—Dr. Richard M. Smith, assistant professor of child hygiene at Harvard University, well known for his child welfare work, received the degree of Doctor of Science from Williams University in June.

Appointments and Promotions.—Dr. William J. Corcoran has been made clinical professor of pediatrics at the Loyola University School of Medicine in Chicago.

Changes in the pediatric faculty of Rush Medical College, the University of Chicago, are: Dr. Arthur H. Parmelee from assistant to associate clinical professor; Dr. Eleanor I. Leslie and Dr. H. N. Sanford from clinical associate to clinical instructor, and Dr. Craig D. Butler from clinical assistant to clinical associate.

Dr. Samuel Goldberg has been appointed associate professor of pediatrics at Temple University School of Medicine, Philadelphia.

SOCIETY NEWS

Convalescent Serum in Poliomyelitis.—The special committee appointed by the New York Academy of Medicine to investigate the value of convalescent serum in the treatment of poliomyelitis, has distributed a supply to a committee of physicians who will assist the attending physician in doing lumbar punctures and will administer the serum in preparalytic cases.

Abstracts from Current Literature

Anatomy and Physiology

On the Glandular Elements in the Posterior Lobe of the Human Hypophysis. Dean Lewis and F. C. Lee, Bull. Johns Hopkins Hosp. **41**:241 (Nov.) 1927.

Lewis and Lee, from a study of serial sections of thirty hypophyses from persons varying in age from birth to 73 years, found gland tissue in the posterior lobe at all ages.

This gland tissue consists of two types: (1) tubuloracemose glands containing colloid material and communicating with the hypophyseal cleft, found in children under 4 years of age, and (2) masses of basophilic cells communicating with the region of the cleft, which are present at all ages but become more numerous with advancing age.

A discussion is given as to the probability of transition from the tubuloracemose glands to the basophilic elements of the posterior lobe during the first few years of life.

Lyttle, New York.

The Effect of Certain Drugs on the Esophagus. P. Guns, Arch. d. mal. de l'app. digestif. **18**:1021 (Nov.) 1929.

The action of atropine, pilocarpine, epinephrine, ergotamine and papaverine on the esophagus was studied by fluoroscopic control. Injections of atropine make the physiologic stops of deglutition more frequent and longer. Pilocarpine accelerates the action of deglutition. Epinephrine and ergotamine have no effect on the innervation of the esophagus. Papaverine produces powerful antiperistaltic movements of the esophagus.

Zentay, St. Louis.

An Abnormal Ridge in the Left Ventricle. L. Brings and A. Spitzer, Virchows Arch. f. path. Anat. **267**:9, 1928.

At autopsy on an infant with congenital heart disease, a connective tissue ridge was found in the left ventricle, on the boundary between the muscular and the membranous portions of the septum. It extended also on to the aortic leaflet of the mitral valve. An explanation for the development of this anomaly is given.

B. R. Lovett.

Anatomic Changes in the Kidneys of Infants. L. Schwarz, Virchows Arch. f. path. Anat. **267**:654, 1928.

Histologic examination of the kidneys of infants revealed inflammatory and infiltrative changes regularly associated with pneumonias. These were similar to the changes described by Schridde and Councilmann in scarlet fever, and consisted of progressive stages: round cell collections in the capillaries, interstitial infiltration of lymphocytes or of plasma cells, and finally connective tissue scars. They occurred in infants dying in the fourth week of life or later, at which time pyuria also was most frequently observed. Inflammatory and infiltrative renal changes were rarely found under three weeks, and then were chiefly of lymphatic nature. They were frequently associated with disease in the mother. The glomerular changes described by Herxheimer were observed in 30 per cent of cases in the first three weeks, and 100 per cent of infants over that age with inflammatory renal changes. Since in almost all instances adequate anatomic basis for the change was found, the view of Herxheimer that it is a congenital malformation could not be supported.

B. R. Lovett.

Pathology, Bacteriology and Biochemistry

A Study of the Action of Mercurochrome, of Horse Serum and of Mixtures Thereof on Pneumococcus Infections in Mice. J. H. Hill and M. G. Ellis, Bull. Johns Hopkins Hosp. **44**:40 (Jan.) 1929.

Series of mice, inoculated with various dilutions of pneumococcus cultures, were treated with mercurochrome-220 soluble alone, with horse serum alone and with mixtures of mercurochrome and serum. The following results were obtained: 1. Mercurochrome alone had definite therapeutic action, when used in dosages of from 15 to 50 mg. per kilogram of weight; better results were obtained with moderate doses than with 100 mg. per kilogram of weight. In the many series of animals studied, from 0 to 40 per cent of the animals treated with mercurochrome survived, although the inoculations were generally many times the lethal dose. In tests in which treatment consisted of 0.3 cc. of a 1:1,000 solution of mercurochrome plus 0.2 cc. of a salt solution, 16.6 per cent of the 120 mice that were so treated immediately after inoculation lived; 10 per cent survived when treatment was delayed one hour after inoculation.

2. Normal horse serum had marked protective action against culture dilutions of 1:1,000,000 or higher. Of the 440 mice treated immediately after inoculation with 0.2 cc. of serum plus 0.3 cc. of salt solution, 22.7 per cent lived.

3. Mice treated with mixtures of mercurochrome and serum showed a markedly favorable therapeutic response as compared with mice receiving either drug or serum alone. One hundred and seventy-three, or 42.8 per cent, of the 404 mice treated with a mixture of 0.3 cc. of a 1:1,000 dilution of mercurochrome and 0.2 cc. of serum lived, as compared with 16.6 per cent saved by the drug alone or 22.7 per cent saved by serum alone. While a statistical analysis shows that the differences between the results with drug alone and serum alone are not significant, valid comparisons may be made between the results with drug alone and the combined treatment and between serum alone and the combined treatment.

4. The therapeutic action shown by mercurochrome and by normal horse serum separately and by the mixture is unrelated to direct germicidal action, as evidenced by the failure of in vitro mixtures of culture dilutions with these substances to show any diminution in virulence.

Lyttle, New York.

Relation of Streptococci to the Spinal Fluid in Experimental Poliomyelitis. P. K. Olitsky, C. P. Rhoads and P. H. Long, J. A. M. A. **92**:1725 (May 25) 1929.

The authors were unable to demonstrate streptococci in the spinal fluid of monkeys showing characteristic experimental poliomyelitis, or in Rosenow's yeast medium cultures. The properties of a streptococcus isolated by Rosenow from the spinal fluid of patients with poliomyelitis correspond in essential characteristics with those of a streptococcus obtained from the brain of a normal monkey and from the air of the laboratory. Inoculation of Rosenow's streptococcus into animals resistant to the virus of poliomyelitis induces a purulent meningo-encephalitis such as is often associated with streptococcic septicemia. The microscopic appearance of the brain of such rabbits differs essentially from that of a man or a monkey with poliomyelitis. Inoculation of the streptococcus intracerebrally in monkeys gives the same reaction in normal animals and in those which have recovered from poliomyelitis, a fact that is in direct conflict with the susceptibility of normal, and the insusceptibility of recovered, monkeys, to the virus of poliomyelitis. In the former instance, the microscopic changes are those of an acute purulent meningitis. The authors believe that these observations support the view that the streptococcus cannot be regarded as identical with the filtrable virus of poliomyelitis.

Bonar, Salt Lake City.

IV. Influence of Light Environment on Normal Rabbits; Calcium and Inorganic Phosphorus in the Blood of Rabbits. W. H. Brown, J. Exper. Med. **49**:103 (Jan.) 1929.

The chemical equilibrium of the blood was definitely affected by keeping rabbits under varying light conditions (neon light and darkness). The effects could be correlated with differences in organic constitution and with certain differences in functional activity which involved nutrition, growth and the proliferative activity of the hair follicles.

Jamieson, Detroit.

Effect of Low Temperatures on Diphtheria Toxin-Antitoxin. Elliott S. Robinson and Benjamin White, J. Immunol. **15**:381, 1928.

Enough evidence is available to justify the statement that under certain conditions some toxin-antitoxin mixtures will become toxic when frozen. These conditions are, so far as they have been determined, the persistence of low temperatures, during more than a minimum period, on toxin-antitoxin mixtures of certain concentrations, containing phenol or tricresol, and possessing other as yet undetermined characteristics. To this should be added the possibility that the phenomenon is in part, if not entirely, one of dissociation of toxin and antitoxin and only in part, if at all, one of destruction of antitoxin.

[Arch. Path.]

Rheumatic Fever. 2. Allergic Reactions with a Toxin-Producing Strain of the Nonmethemoglobin-Forming Streptococcus Isolated from Rheumatic Fever. Konrad E. Birkhaug, J. Infect. Dis. **43**:280, 1928.

Guinea-pigs and rabbits sensitized to the nonmethemoglobin-forming streptococcus isolated from patients with rheumatic fever may be rendered cutaneously hypersensitive to filtrates of cultures of this organism. A brief period of specificity in the sensitive state is recorded. This period is shortly followed by a sensitive state that is nonspecific. During this phase of the cutaneous reactions, the allergenic property of the filtrate can be nullified completely with specific antiserums. After the end of the cutaneous allergy of this first phase, continued sensitization of the animals with living nonmethemoglobin-forming streptococci produces the reappearance of cutaneous allergy. During the second phase, the reactions of allergy are nonspecific and the allergic principle of the filtrate is nonneutralizable with specific antiserums. For this phase, filtrates heated at 98 C. for four hours are not inactivated as allergic substances. Heterogeneity in the cutaneous responses of patients with rheumatic fever to filtrates of the nonmethemoglobin-forming streptococcus and to certain strains of *Streptococcus viridans* might be explained on the basis of prolonged sensitization to any one dominant strain of the nonhemolytic streptococci. Desensitization of bacterially hyperallergic guinea-pigs and rabbits was accomplished during the second phase of cutaneous allergy by intracardial or intravenous injections of bacterial filtrates.

[Arch. Path.]

The Thermal Death Point of Brucella Abortus in Milk. Ruth Boak and C. M. Carpenter, J. Infect. Dis. **43**:327, 1928.

The thermal death point of eight strains of *Brucella abortus* of porcine, human and bovine origin grown in milk was variable. The porcine strains was most resistant. An exposure of fifteen minutes at 140 F. (60 C.) destroyed the human and bovine cultures that were examined. The porcine strain, however, was still viable at this temperature.

The injection of guinea-pigs was more reliable than cultures for determining the viability of *Brucella abortus* in milk.

[Arch. Path.]

RECENT ADVANCES IN PHARMACOLOGY. CARL A. DRAGSTEDT, Northwest Med. **28**:49 (Feb.) 1929.

Dragstedt considers:

1. The dissociation of the oxytocic and pressor factors present in pituitary.

2. Barbital in controlling the convulsions of cocaine poisoning.

3. New cardiovascular and respiratory stimulants, such as metrazol, homocamfin and alpha-lobeline, the value of none of which has been established.

4. Ephedrine and its preparations.

5. The use of kanthine derivatives in angina pectoris, particularly theophylline sodio-acetate.

6. The discovery that digitalis decreases rather than increases the cardiac output.

7. Researches in the field of phytopharmacology.

8. Discovery that there is no tolerance developed to the stimulating effect of morphine, but only to its narcotizing effect.

9. A more optimistic attitude toward chemotherapy. SCOTT, Philadelphia.

NATURAL ACQUIREMENT OF IMMUNITY. W. W. C. TOPLEY, Lancet **1**:1337 (June 29) 1929.

The author's conclusions are:

1. The acquirement of specific antibacterial immunity depends, in the main, on the production of specific antibodies which sensitize the bacterial cell. The sensitized bacteria are more readily ingested by the phagocytic cells of the tissues and, in some cases at least, are acted on by other noncellular agents which destroy them or inhibit their invasive activity. These specific antibodies are themselves produced or increased significantly in amount in response to the entry into the tissues of bacteria that contain the corresponding antigens.

2. These antibodies are of one kind only, in the sense that for each antigen there is one and only one corresponding antibody.

3. In any pathogenic bacterium, on the other hand, there are several antigens; these are of unequal importance in immunity reactions in vivo. The presence of the antibody corresponding to one particular antigenic component may profoundly modify the course of events in favor of the host. The presence of the antibody corresponding to another antigenic component may be without effect. This difference in the immunologic significance of different antigens probably depends on their position in the bacterial cell. The acquirement of specific antibacterial immunity depends on the production of antibodies acting on the effective bacterial antigens.

4. The condition of an animal that has acquired immunity differs from that of a normal animal not only in the presence of the effective specific antibody in its blood and body fluids but in the readiness with which this antibody is produced in response to further stimuli, and perhaps in the presence of fixed antibody in certain cells and tissues.

5. During the process of natural immunization, foci of infection are established in the tissues and may persist for long periods of time. The animal is, relatively immune, however, to fresh infection from without and to the spread of infection beyond the localized foci. This specific immunity depends on the maintenance of the clearing mechanism of the tissues, at a high level, which ensures the prompt removal of any bacteria that gain access to the lymphatics or the blood vessels. It may be overcome either by massive infection, from without or by the action of various nonspecific factors that cause a spread of the infection from latent foci.

6. The available evidence does not suggest that the bacteria in the latent foci become avirulent. In some cases at least, they retain their full virulence for long periods of time.

LANGMANN, New York.

PERMEABILITY OF THE BLOOD AND THE CEREBROSPINAL FLUID OF INFANTS FOR BROMINE. F. KRAUSE, Arch. f. Kinderh. **86**:254 (March 28) 1929.

Krause used Walter's method of giving 0.06 Gm. per kilogram of sodium bromide by mouth three times daily for five days and then estimating the bromide content of the blood serum and the spinal fluid of sixty-four children from 1 to 16 months of age. He found that the so-called bromide quotient was lower in dystrophic children than in normal children, this being entirely a function of the permeability of the blood. Particularly low values were obtained in infants with congenital syphilis, pertussis and erythroderma.

SANFORD, Chicago.

BLOOD SERUM PHOSPHATE IN TOXICOSIS. F. KRAUSE and W. SLADCZYK, Arch. f. Kinderh. **86**:266 (March) 1929.

During the months of August, September and October, at the Halle clinic, the normal blood serum phosphorus of children under 13 months of age averaged between 5.5 and 7.2 mg. In toxicosis, blood drawn before treatment and approximately from four to six hours after food was last taken averaged from 8 to 11.2 mg. of phosphorus. After one or two days' treatment, the amount of phosphorus fell to from 3 to 5 mg.; after recovery, it rose to approximately the normal value of from 5.7 to 7.4 mg.

SANFORD, Chicago.

THE INFLUENCE OF ADMINISTRATION OF THYROID ON THE PROTEIN AND FAT METABOLISM. B. KOMMERELL, Biochem. Ztschr. **208**:112 (April 30) 1929.

The administration of thyroid increased the basal metabolic rate in dogs 30.5 per cent. About one third of this increased caloric requirement was supplied by the metabolism of protein, and the rest by the metabolism of fat.

BRAHDY, New York.

CHANGES IN THE SERUM CHOLESTEROL IN ANAPHYLAXIS. J. M. GOLDBERG and W. N. NEKLUDON, Biochem. Ztschr. **208**:285 (May) 1929.

The authors found an increase in the cholesterol content of the serum of rabbits and guinea-pigs after the induction of anaphylactic shock. The increase was observed as early as one minute after the onset of shock and lasted as long as from fifteen to thirty minutes.

BRAHDY, New York.

LOCALIZATION OF COWPOX VACCINE IN THE BLOOD OF VACCINATED GUINEA-PIGS. HACKENTHAL, Deutsche med. Wchnschr. **55**:960 (June 7) 1929.

At a meeting of microbiologists in Berne in 1928, Gins Hackenthal and Kamenschewa reported that the virus of cowpox vaccine is retained in the blood of vaccinated guinea-pigs from two to ten days after vaccination. In the present communication, the author demonstrates the distribution of the virus in the blood. The technic is described in full. The test inoculations were made by the instillation of four portions of sedimented blood to be tested in the scarified cornea of non-vaccinated guinea-pigs. The results were as follows: By the use of fresh citrated blood of nonvaccinated guinea-pigs, no reaction was obtained; fresh citrated blood from vaccinated guinea-pigs gave 80 per cent reactions; the upper portion of the serum of blood sedimented by the technic described, no reactions; with the lower portion of the serum, no reaction; with the portion containing the leukocytes, 95 per cent reactions, and with the portion containing the erythrocytes, 10 per cent reactions.

The author quotes the report of Wilson and Smith which appeared in the *British Journal of Experimental Pathology* (1929, vol. 10), while his work was in progress of preparation. These workers used rabbits, but their results coincide with those of the author.

SCHERER, Duluth.

SEVERE DAMAGE TO RABBITS THROUGH IRRADIATED ERGOSTEROL. R. FISCHL and B. EPSTEIN, Med. Klin. **25**:21 (Jan. 4) 1929.

In the course of experiments on syphilis in rabbits, the animals developed rickets. Irradiated ergosterol was used as treatment. The animals received 5 drops of 1 per cent irradiated ergosterol twice a day. Several of them developed a clouding of the lens that improved promptly on discontinuance of the treatment. The clouding is apparently due to calcium deposits in the substance of the lens. It seems that rabbits are rather sensitive to this drug, and the experiments also seem to prove that irradiated ergosterol is a powerful agent that mobilizes calcium easily. This mobilized calcium may reach undesirable places in the body and may produce serious damage. The authors therefore advise caution in the use of irradiated ergosterol or irradiated milk.

ZENTAY, St. Louis.

RESIDUAL OXYGEN IN EXPERIMENTAL EXSICCOSIS. M. FUKUYAMA, Monatschr. f. Kinderh. **43**:337 (May) 1929.

The author uses the term "Vakatsauerstoff," which is perhaps best translated as residual oxygen, to mean the amount of oxygen required to oxidize entirely all the organic elements in the urine. He gives the chemical technic and in cases of experimental dehydration in animals finds that the amount of oxygen needed is increased. He concludes that dehydration hinders oxidative processes.

GERSTLEY, Chicago.

THE STIMULATION OF THE GROWTH OF BONE BY INJECTIONS OF AN EXTRACT OF BONE. ZAWISCH-OSSENITZ, Wien. klin. Wchnschr. **42**:733 (May 30) 1929.

Continuing work reported in 1926 (*Wien. klin. Wchnschr.* **39**:1301, 1926), the author studied the effects of an aqueous extract of rapidly growing bones. This contains a thermolabile substance which on parenteral injection promotes the deposition of the organic portion of bone, and is therefore distinct from the phosphatose of Robison, which causes deposition of calcium phosphate. As the source of extract, the author used the ephiphyses of calves' bones; he used cats and rabbits as test animals. Since, in this paper, no chemical analyses, only measurements and merely a reference to histologic studies are reported, it is not possible to accept the claims made. It is suggested that the extract might be useful in the treatment for osteopsathyrosis, delayed formation of callus and especially osteogenesis imperfecta in man.

CLAUSEN, Rochester, N. Y.

THE RATE OF DISINTEGRATION OF BLOOD PLATELETS IN NORMAL CHILDREN, IN HEMOPHILIA AND IN THROMBOPENIA. BAAR and SZÉKÉLY, Wien. klin. Wchnschr. **42**:761 (May 30) 1929.

Platelet counts are made on mixtures of blood and urea citrate-sodium citrate solutions at various intervals of time. Normal curves agree closely. The curves in hemophilia approach the normal, but the platelets in thrombopenia are more resistant than normal.

CLAUSEN, Rochester, N. Y.

SULPHUR IN THE BLOOD OF CHILDREN. P. BOSIO, Pediatria **37**:399, 1929.

The author, employing Gauvin's method, has studied the behavior of the sulphur fractions (neutral and acid) in the blood of healthy children and concludes that the average content of total sulphur is about 0.1 Gm. per thousand, of which 75.55 per cent is acid and 24.45 per cent neutral. In older children, the figures approximate those of the adult; in children between 4 and 6 the total amount of sulphur is about 12 per cent higher.

In children with tracheobronchial adenopathy without fever, the total amount of sulphur is higher, and the neutral sulphur reaches an average of 31 per cent of the total. About the same thing happens in the stationary forms of pulmonary

tuberculosis. The highest content of total sulphur, when the increase is almost entirely in the neutral fraction (up to 100 per cent more than the normal), occurs when there is interference with respiration.

In the several stages of typhoid, the observations were of no particular significance.

SALA, New York.

EFFECT OF ULTRAVIOLET IRRADIATION ON THE ANTIBODY FORMATION. YOSHIHISA HASEBE, J. Pediat. (Tokyo), March 20, 1929, no. 346, p. 520.

Hasebe found that in rabbits the value of antibody does not increase after it reaches its maximum as the result of repeated intravenous injections of a 10 per cent suspension of red blood cells from the goat, unless some other treatment intervenes. The antibody value was determined by the estimating of the amount of agglutinin, hemolysin and precipitin. The ultraviolet irradiation in such an animal causes a marked increase in antibody values, often far exceeding that of its maximal value found at the initial determination. The dosage of such an irradiation, however; must not be large, as the antibody values increase only when relatively small dosage is applied. The dosage must be calculated properly according to the thickness of fur.

KATO, Los Angeles.

THE EFFECT OF ACIDS AND FRUIT JUICES ON THE BEHAVIOR OF EXCISED INTESTINE. HISASHI SATO, J. Pediat. (Tokyo), April 20, 1929, no. 347, p. 694.

The author used pieces of the excised intestine, 3 cm. in length, taken at the following levels; the duodenum, immediately below the pylorus, the jejunum, ileum and colon. The animals used were rats of normal health and habits. The excised intestine was attached at one end to an apparatus for the introduction of various testing fluids, and the other end was connected with a recording machine; the entire tissue was kept at normal by temperature and immersed in Tyrode's solution, and a supply of oxygen was kept up by means of a small tube introduced into the solution. The acids used were acetic, lactic, propionic, formic, citric, butyric, succinic, tartaris and hydrochloric, in strengths of from 1 to 5 per cent. In weaker strengths the acids require too long a time to elicit the reaction to facilitate the experimental work. The fruit juices were taken mostly from citrus fruit. All the reagents were titrated by means of tenth-normal sodium hydrate solution, and their p_H values were determined by the colorimetric method. The effect of these acids and juices was for the most part that of excitation rather than that of inhibition. The jejunum was the least affected, with most variable results. When acids of greater strengths were used, the degree of excitation increased, although some exceptions were seen. In the reading of results, the macroscopic observation of the intestine is as important as the tracings obtained. In the duodenum, the movements of the intestine were often backward, that is, toward the stomach. The colon was the most reactive portion of the intestine toward the reagents used. The effect of organic acids was irregular as compared with that of inorganic acids, and hence the statement of Lurje is contradicted. Such acids as are ordinarily ingested into the alimentary tract cannot be the cause of diarrhea or vomiting, unless they somehow become greater in strength after the introduction. If acids and juices of unripe fruit are introduced by mouth in great strength, they can be the cause of such digestive disturbances.

KATO, Los Angeles.

Nutrition

STUDIES IN RICKETS: III. PREVENTION BY MEANS OF ULTRAVIOLET IRRADIATION. THEODORE K. SELKUK, J. VICTOR GREENBAUM and A. GRAEME MITCHELL, J. A. M. A. **91**:2057 (Dec. 29) 1928.

Three hundred and eighty-six infants were studied to determine whether ultraviolet irradiation was a practicable method to use for the prevention of rickets. No

infant receiving more than sixty-five minutes' total treatment up to 8 months of age developed rickets. Most of those developing rickets had intervals of two or more months without treatment. Eleven minutes' total irradiation a month, without other antirachitic measures, prevented rickets in 98 per cent of the infants studied. It was therefore concluded that a small amount of ultraviolet irradiation from an efficient artificial source was a practicable method of preventing rickets in the infant if it was started early and given regularly.

BONAR, Salt Lake City.

THE CURD AND THE BUFFER IN INFANT FEEDING. JOSEPH BRENNEMANN, J. A. M. A. **92**:364 (Feb. 2) 1929.

The author reports the progress of an investigation being carried on at the Children's Memorial Hospital, Chicago, which has as its objective a critical clinical investigation of the validity of the theories advanced as to the reason for the superiority of acid milk over sweet milk. One series of children was given a preparation of evaporated milk, karo corn syrup and lactic acid, while another series was given a mixture that was identical except for the omission of lactic acid. The only deduction warranted from this limited investigation would seem to be that the general run of infants under 18 months of age, during a period when parenteral infections, chiefly of the respiratory tract, were prevalent, did not show any appreciably different reaction to acidified and nonacidified evaporated milk that had been diluted one-half and fortified with 10 per cent karo corn syrup.

BONAR, Salt Lake City.

QUARTZ LAMP THERAPY IN HUMAN RICKETS AND RACHITIC SPASMOPHILIA.. HENRY J. GERSTENBERGER and J. I. HARTMAN, J. A. M. A. **92**:367 (Feb. 2) 1929.

Weekly exposures to the ultraviolet rays produced by the quartz lamp in doses of 1 erythema unit, as determined by the method of Rost and Keller, bring about healing in practically the same time as that required in the heavier schedules generally used at present. Because of the simplicity and economy of this arrangement and because of the slight change produced by such exposures to the skin, this method is advocated in the cure and prevention of rickets and rachitic spasmophilia.

BONAR, Salt Lake City.

ROUTINE USE OF VITAMIN B FACTOR IN INFANT FEEDING. ROGER H. DENNETT, J. A. M. A. **92**:769 (March 9) 1929.

The author concurs with Macy and Hoobler that cow's milk and, in some instances, breast milk do not contain the optimal quantity of vitamin B, and that some of this factor should be added as a routine to the food of all bottle fed infants. One-third ounce by weight or one level tablespoonful of wheat germ sugar provides as much of the antineuritic factor as 1 quart of milk, and as much of the pellagra preventing factor as 10 ounces of milk, and is more palatable than yeast. The author is of the opinion that from ⅓ to 1 ounce should be given daily to every bottle fed infant throughout the first year of life.

BONAR, Salt Lake City.

RELATION OF THE ALTITUDE OF THE SUN TO ITS ANTIRACHITIC EFFECT. FREDERICK F. TISDALL and ALAN BROWN, J. A. M. A. **92**:860 (March 16) 1929.

A marked increase in the antirachitic effect of sunshine appears when the sun reaches an altitude of 35 degrees or more. Rickets is uncommon or exists in a mild form in those places where the minimum seasonal altitude of the sun comes within this limit, and the converse is true where the sun's altitude is below 35 degrees for some months of the year. The period of the year during which rickets will probably develop can be calculated for any city in the world. The duration

of this period may be altered if patients are prevented from enjoying highly effective sunshine because of inclement spring weather or other factors.

BONAR, Salt Lake City.

CALCINOSIS AND SCLERODERMA IN A CHILD TREATED BY KETOGENIC DIET. R. L. J. KENNEDY, M. Clin. N. Amer. **12**:1655 (May) 1929.

Kennedy reports a case of calcinosis and scleroderma in a child, aged 6 years, who apparently definitely improved while being kept on a ketogenic diet. Although the etiology and pathogenesis of this condition are unknown, the following observations suggest a reasonable basis for such treatment: fractured bones of diabetic patients heal slowly and with difficulty, presumably because acidotic metabolism hinders the calcification of newly formed bone; the metabolism of rachitic infants is acidotic, and this acidosis is an important factor in preventing the deposit of calcium salts in the zone of ossification; certain observations on epileptic children on ketogenic diets have shown that the output of calcium and phosphorus exceded the intake.

SMITH, Ogden, Utah.

COD LIVER OIL AND ACTIVATED ERGOSTEROL THERAPY. NORMAN W. CLIEN, Northwest Med. **28**:232 (May) 1929.

Clien discusses the wide limits of dosage of cod liver oil and the variations in its antirachitic potency. He compares this with the irradiated ergosterol solutions and cod liver oils fortified with irradiated ergosterol. He urges the prescribing of cod liver oil or known potency and the standardization of its dosage.

SCOTT, Philadelphia.

VITAMIN B. ROBERT HUGH ROSE, M. J. & Rec. **129**:563 (May 15) 1929.

Vitamin B is antineuritic and cures patients with beri-beri within a few months unless the disease is far advanced. Associated with vitamin B there is probably another vitamin that is curative in pellagra. Vitamin B is lost in the water in which vegetables are cooked, but dry cooking does not destroy it. It is destroyed by alkalis but not readily by acids. It is contained in many vegetables, fruits, whole grain seeds, eggs and milk. It is chiefly essential in two ways, as an antineuritic and as a stimulant to growth.

WILLIAMSON, New Orleans.

LABORATORY CONTROL OF MILK UNDER THE NEW STATE CODE. MORRIS MASLON, New York State J. Med. **29**:85 (Jan. 15) 1929.

The local health officer must have bacterial counts made by an approved laboratory before he can issue a permit for the sale of milk or cream. The milk is graded on the average of three bacterial counts, each from a sample taken on a different day. Examination must be made at least every three months.

The code calls for the following grades, showing not more than the stated number of colonies, in the final count: pasteurized grade A, 30,000; certified, 10,000; pasteurized grade B, 50,000; raw grade A, 30,000, and raw grade B, 30,000.

AIKMAN, Rochester, N. Y.

THE CARBOHYDRATE CONTENT OF FOODS. R. A. MCCANCE and R. D. LAWRENCE, Medical Research Council, bull. no. 135, 1929.

Starch is the only polysaccharide hydrolized by mammalian digestive enzymes and available as carbohydrate for metabolism. All vegetable foods contain other polysaccharides, and these are not attacked by enzymes. They are broken down by symbiotic micro-organisms in the intestines. The products formed and absorbed are not sugars but fatty acids, so that these polysaccharides cannot be regarded as supplying the host with carbohydrate. These polysaccharides act as laxatives. In all, a most important factor is the local intestinal stimulation set up by their

breakdown products. Some increase the bulk of the feces by passing through the intestines unchanged, or by their property of holding water (agar-agar). Others stimulate local peristalsis by their rough physical form.

SANFORD, Chicago.

THE USE OF SUBCUTANEOUS INJECTIONS OF OXYGEN TO IMPROVE THE APPETITE AND THE NUTRITION IN THE INFANT. M. BRIAND, Bull. Soc. de pédiat. de Paris **27**:77 (Jan.) 1929.

In the treatment of pertussis injections of oxygen did not give startling cures, but it was noted that there was less loss of weight in the children who received the injections than in those treated by other means. Many infants maintained their weight throughout the disease, and this was not entirely due to cessation of vomiting. So, injections of oxygen were tried on infants with poor appetite and distaste for milk who failed to gain in weight. In every case, the result was successful. Five cases are cited of infants who were not gaining and in whose regimen the only change made was the addition of oxygen injections, when they at once began to gain in weight. The amount of oxygen injected was of secondary importance; 100 cc. gave no better results than from 40 to 50 cc. Fifty cubic centimeters injected every two or three days according to the rapidity of absorption is recommended for infants with poor appetite and loss of weight or failure to gain in weight, when no definite pathologic condition is found to account for the situation. The authors are conducting a study to determine just how these injections act in the body.

BENJAMIN, Montreal.

THE PROCESS OF ADIPOLYSIS IN THE COURSE OF LOSS OF WEIGHT IN INFANCY. H. DORLENCOURT and FALCON, Bull. Soc. de pédiat. de Paris **27**:82 (Jan.) 1929.

In malnutrition the carbohydrate in the body in the form of glycogen is first used up, then the fat, and lastly the protein. The fat of the body disappears in a definite anatomic sequence: first the subcutaneous fat is used up, beginning on the abdomen, then that on the chest, back, loins, arms, forearms, legs, buttocks and lastly on the face, and during this period the perivesceral, epiploic and mesenteric fat is also used up. When wasting goes on until death only from 6.75 to 9 per cent of the normal fat of the body remains. The definite sequence in the areas of loss of fat is due to a variation in composition. By determining the saponification index, the iodine index and the melting point of various areas of fat, it was found that these three values were altered in each location of the body according to whether the infants were well nourished, hypothreptic or athreptic. The more nonsaturated fatty acid (oleic) present in the fat as compared with the amount of saturated fatty acids (stearic, palmitic, etc.) the sooner does the body call on that fat when necessary.

BENJAMIN, Montreal.

AN ATTEMPT TO SUBSTITUTE ACIDIFIED MILK FOR BUTTERMILK IN THE FEEDING OF DEBILITATED AND HYPOTHREPTIC NEWLY BORN INFANTS. A. B. MARFAN and M. CHEVALLEY, Bull. Soc. de pédiat. de Paris **26**:239 (May) 1928.

The authors fed nine very young hypothreptic infants on (*a*) lactic acid milk prepared according to Marriott (*J. A. M. A.* **73**:1173 [Oct. 18] 1919), using a malt extract instead of corn syrup, and (*b*) buttermilk or human milk (their feedings furnished from 95 to 140 calories per kilogram of body weight per day). They conclude that lactic acid milk is a frequent cause of vomiting and failure to gain in weight. In two cases, their results with diluted lactic acid milk are no more encouraging.

CLAUSEN, Rochester, N. Y.

TREATMENT OF ACID DIARRHEAS BY ADSORBENTS. H. SLOBOSIANO, Nourrisson **17**:93 (March) 1929.

In the treatment for diarrhea with acid stools, occurring in breast-fed infants, a formula is proposed consisting of kaolin, 15 Gm.; tribasic calcium phosphate, 15 Gm.; benzoate of soda, 1.5 Gm.; syrup, 30 cc., and distilled water, 270 cc. The directions call for 10 cc. five times a day. After a few days the stools become alkaline and normal in frequency and consistency. The sodium benzoate is added as a preservative.

McCLELLAND, Cleveland.

INFANT FEEDING. A. B. MARFAN, Nourrisson **17**:129 (May) 1929.

Digestive disturbances in infants receiving breast milk only are seldom severe and are usually of the parenteral variety. This is especially true in cases of diarrhea accompanied by fever. If the diarrhea is severe enough to produce anhydremia, Marfan believes that rehydration can best be accomplished by the administration of water by mouth, with the use of either a teaspoon or a medicine dropper rather than a bottle. Infants under the age of 1 year should receive at least 150 cc. per kilogram of body weight.

McCLELLAND, Cleveland.

VALUE OF PEANUT FLOUR IN INFANT FEEDING. M. BOIGEY, Nourrisson **17**: 145 (May) 1929.

Analyses of flour made from peanuts show high values in protein (58.2 per cent) and in fat (6.09 per cent). The caloric value for 100 Gm. averages 360 calories. The flour its also rich in phosphorus, lecithin, cholesterol and vitamin A. In digestibility, it compares favorably with wheat flour. Both in laboratory animals and in infants, the author has found peanut flour of value in promoting growth and rapid convalescence.

McCLELLAND, Cleveland.

THE SULPHUR IN HUMAN AND COW'S MILK. P. BOSIO, Riv. di clin. pediat. **27**:364 (May) 1929.

The accompanying table summarizes the author's analyses:

Sulphur in Human and Cow's Milk

	Total Sulphur, Gm. per 1,000 Gm. of Milk	Neutral Sulphur, Gm. per 1,000 Gm. of Milk	Number of Determinations
Human colostrum: Second day	0.146	0.047	2
Third day	0.059	0.017	2
Fifth day	0.063	0.010	2
Human Milk: Average	0.059	0.013	13
Maximum	0.100	0.020	..
Minimum	0.028	0.005	..
Cow's colostrum	0.077	0.023	4
Cow's milk	0.052	0.011	9
Sheep's colostrum	0.036	0.011	3

The author concludes that sulphur is present in relatively large amounts in human colostrum; this amount diminishes as milk appears.

HIGGINS, Boston.

INCREASE OF TOXICOSIS AMONG INFANTS IN GERMANY DURING THE SUMMER OF 1928. F. GOEBEL, Arch. f. Kinderh. **86**:241 (March 28) 1929.

Goebel observed forty-seven cases of toxicosis in the Halle clinic in 1928, compared with seven in 1927, and eleven in 1926. The temperature has a great effect on the number of cases, which increase in warm summers. The warmest localities will show the greatest number of cases. The mortality depends entirely on the treatment, which depends, in turn, on the severity of the case. In the so-called light cases, 10 per cent rice water and albumin milk will suffice, but in the more severe cases the prognosis is unfavorable unless breast milk is obtained.

SANFORD, Chicago.

IRRADIATED MILK OR IRRADIATED ERGOSTEROL? W. STOELTZNER, München. med. Wchnschr. **76**:920 (May 31) 1929.

Treatment with irradiation for rickets has developed recently along two lines, that is, by means of irradiation of food (principally milk) and by irradiation of ergosterins.

The fact that these methods should be followed does not detract from the discovery of Huldschinsky that irradiation of the rachitic child cures the disease. It records progress.

Whether irradiated milk or irradiated ergosterol should be used is yet to be determined. The author realizes that ergosterin can be highly charged, and that large doses have led to abnormal calcification and parenchymatous degeneration. Irradiated ergosterol has the advantage over milk in that it is cheap, readily accessible and efficient, and that the dosage can be accurately measured.

SCHORER, Kansas City, Mo.

THE BIOLOGIC EFFECTS OF FATS AND CHOCOLATE IRRADIATED BY ULTRAVIOLET LIGHT. O. RIED, Wien. klin. Wchnschr. **42**:896 (July 4) 1929.

The author's original purpose was to confer antirachitic properties on chocolate by irradiation. He claims in this preliminary report to have attained results, a growth-promoting effect, in particular, which cannot be explained by the production in the chocolate of vitamin D only. Since no statement is made concerning the type of diet given to his experimental animals, the reviewer cannot accept this claim. Nothing is said about the source of light, nor the exclusion of oxygen during the irradiation. Much emphasis is laid on a supposed photo-activity conferred by irradiation on the "fats," presumably of the chocolate. No reference is made to similar experiments done several years ago in America with cod liver oil, which showed this activity to be in all probability the Russell effect. The irradiated cholocate may be bought from a Vienna manufacturer.

CLAUSEN, Rochester, N. Y.

THERAPEUTIC EXPERIMENTS WITH CHOCOLATE IRRADIATED WITH ULTRAVIOLET LIGHT. H. KRASSO, Wien. klin. Wchnschr. **42**:898 (July 4) 1929.

For long periods, the author administered daily doses of about 100 Gm. of the irradiated milk chocolate described by Ried (*Wien. klin. Wchnschr.* **42**:896, 1929) to patients in the clinic of Kovacs. Great improvement in appetite was noticed in practically all cases; considerable gain in weight was made, particularly by patients suffering from fibrous phthisis. Apparently no control was attempted by giving unirradiated chocolate, and no mention is made of the number of cases.

CLAUSEN, Rochester, N. Y.

NUTRITION OF TWINS FROM ONE OVUM. J. BERNHEIM-KARRER, Ztschr. f. Kinderh. **47**:427 (March 23) 1929.

In three of five pairs of twins from one ovum nourished with raw and cooked human milk, there was a slight advantage in the bactericidal characteristic of the blood serum. Infants fed on raw milk were not better protected against grippal infections than those fed with cooked milk. The same fact was observed in regard to infection of the urinary tract with the colon bacillus.

EMERSON, Boston.

AN EXPERIMENTAL STUDY OF EXCRETION OF MORPHINE IN THE BREAST MILK. SENZABURO ISODA, J. Pediat. (Tokyo), April 20, 1929, no. 347, p. 716.

Experimenting on nursing dogs, the author injected morphine hydrochloride in varying amounts into the mother and studied the behavior of puppies. He came to the conclusion that when a lethal dose of morphine hydrochloride is given to the mother hypodermically, the puppies present a comatose condition, with difficulty

in locomotion and severe salivation. They usually recover in the course of time. It appears that the excretion of morphine in such cases is relatively large in amount. If smaller amounts of the same drug are given, there seems to be no effect on the puppies, even on the repetition of the dose. The puppies continue to grow in a normal manner when fed by the breast milk of the mother which is receiving repeated doses of the small amounts of morphine.

KATO, Los Angeles.

PELLAGRA AS OBSERVED IN CHINA: WITH A REPORT ON ONE CASE IN PEIPING. MU JUI-WU, Nat. M. J. China **8**:229 (June) 1927.

Pellagra has been shown to exist in China. Mu Jui-Wu, in describing eight cases seen in Peiping Union Medical College, points out that a large majority of the population live on an extremely restricted diet and that it is difficult to understand why the condition is not more frequent.

LUCAS, San Francisco.

Prenatal Conditions

CONGENITAL ATRESIA AND STENOSIS OF THE BILE DUCTS. WILLIAM E. LADD, J. A. M. A. **91**:1082 (Oct. 13) 1928.

Congenital absence of the bile ducts occurs with sufficient frequency to be more than a pathologic curiosity, and it is unfortunate that many textbooks give the impression that no treatment can be undertaken with any hope of success. Congenital atresia and stenosis are due to faulty development. The time at which an operation should be undertaken is when the diagnosis seems reasonably certain, before wasting or intercurrent infection has set in and when medical treatment has failed. Surgical treatment may be successful if either the gallbladder or the common duct has a patent connection with the liver. Exploration should be done in these cases much more frequently than in the past. A series of eight cases, in which the ages of the patients ranged from 3 weeks to 5 years, is reported; a successful operation was performed in six.

BONAR, Salt Lake City.

CONGENITAL DIVERTICULUM OF THE ESOPHAGUS. LESLIE V. RUSH and C. L. STINGILY, South. M. J. **22**:547, 1929.

Ante mortem, the sac of the diverticulum appeared to communicate with the trachea rather than with the esophagus.

The globular sac proved to communicate with the esophagus by a narrow, valvelike opening which freely allowed the entrance of air but rendered its exit difficult. The sac at first was filled with air, but eventually with pus. The injection of iodized poppy seed oil 40 per cent permitted visualization of the contour of the sac.

Death resulted on the twentieth day, from aspiration pneumonia.

SCHLUTZ, Minneapolis.

PRIMOGENITURE: IS IT A FACTOR IN THE PRODUCTION OF DEVELOPMENTAL ANOMALIES? MADGE THURLOW MACKLIN, Lancet **1**:971 (May 11) 1929.

The author collected reports of 600 cases of hereditary defects occurring in 286 families comprised of 1,585 members in which the order of birth was stated. The number of affected children gradually diminishes until the thirteenth child is reached, when there is a sudden rise in the curve. The author found that there was no more tendency for the first-born to be affected with these inheritable diseases than for any of the other members of the family.

One thousand cases of congenital defects in which there was no family history of similar conditions were also studied, 28 per cent of the total membership and 29 per cent of the affected population taking first place. The same number of fourth and seventh children are affected as of first. "This strongly suggests that the first born is not in such a dangerous position as has been supposed."

The author claims that the reason Still arrived at exactly the opposite conclusion is that he plotted his curve of place-in-family from statistics based on a population of which his patients were not a part. Cases from private practice show a much higher percentage of first-born children than does the population as a whole, since families are smaller in the wealthier classes. Furthermore, the appearance of one malformed child is often the cause of restricting the family.

LANGMANN, New York.

CONGENITAL DEFORMITY OF THE ARM (HEMIECTROMELIAL) WITH TOTAL ABSENCE OF HAND AND RUDIMENTARY RADIUS AND ULNA. S. SEGAL, Proc. Roy. Soc. Med. **22**:643 (March) 1929.

A case was reported in a boy, aged 3½ years. The report is accompanied by a photograph of the deformity and an x-ray picture of the bones of the left upper extremity, showing the rudimentary radius and ulna. They are 2 inches (5 cm.) in length. The lower ends of the radius are in contact and appear to articulate.

WILLIAMSON, New Orleans.

ARACHNODACTYLIA. A. CARRAU, Nourrisson **17**:82 (March) 1929.

The case described occurred in a girl, aged 2 years and 9 months. There was nothing of importance in the history. In addition to the thin, elongated extremities, the child had a marked kyphoscoliosis, bilateral congenital dislocation of the hips, clubfoot, upward dislocation of the patellae and a poorly developed and relaxed musculature. Subacute bronchopneumonia, secondary anemia and mental deficiency were also present. As an explanation for this uncommon congenital defect, the author suggests that a toxi-infectious state in the mother during the early stages of pregnancy could permanently injure the undifferentiated mesoderm of the fetus, causing irreparable damage to future muscles, bones and cartilage. The bibliography contains the reports of twenty other cases, including one American case associated with congenital disease of the heart (Piper and Irvine-Jones: Arachnodactylia and Its Association with Congenital Heart Disease, AM. J. DIS. CHILD. **31**:882 [June] 1926).

McCLELLAND, Cleveland.

CONGENITAL DEXTROCARDIA. M. MAXACHVILI, Nourrisson **17**:95 (March) 1925.

The case reported occurred in a girl, aged 10 months, who had been under observation since she was 12 days of age. The dextrocardia was not associated with a situs inversus, nor was there any evidence of other cardiac anomaly. The roentgenogram showed a mirror image of a normally placed heart, thus proving a complete inversion of the cardiac cavities instead of the more common cardiac rotation. These data serve to classify this case as one of the pure, isolated dextrocardia without other cardiac defect. The condition is rare, as the literature contains the report of only four other cases. Dr. Maud Abbott, in her article on congenital heart disease in Osler and McCrae's "System of Medicine," referred to only four cases of this rare type of congenital dextrocardia which she culled from an extensive review of the literature.

McCLELLAND, Cleveland.

CONGENITAL DILATATION OF THE UPPER URINARY PASSAGES. IVAN SPITZER, Monatschr. f. Kinderh. **43**:247 (May) 1929.

Spitzer presents the case report of a boy, aged 8 years, who came to the hospital with symptoms of severe cystitis. He did not respond to treatment and eventually succumbed to uremia. Autopsy showed an enlarged bladder with ureters dilated to the size of the small intestine and dilated pelves of the kidney. The condition is, of course, a congenital malformation.

GERSTLEY, Chicago.

ATRESIA OF THE ESOPHAGUS: IX. REPORT OF THREE CASES. HANS TEMMING, Ztschr. f. Kinderh. **47**:443 (March 23) 1929.

In case 1, the esophagus, ending blindly, was connected by a fistula with the trachea from which a normal esophagus opened. In case 2, there was atresia of the esophagus at the height of the bifurcation of the trachea with a continuation of the trachea as an esophagus to the stomach. In case 3, an infant who also had an imperforate anus had atresia of the esophagus, as demonstrated by x-ray pictures and by sound, although the diagnosis was not confirmed at autopsy.

CONGENITAL SYNOSTOSIS OF THE MAXILLA AND MANDIBULA: X. JOHANN PETHEÖ, Ztschr. f. Kinderh. **47**:447 (March 23) 1929.

Petheö reports a congenital synostosis of the maxilla and mandibula in an infant one-half day of age, who could not cry, suck or open its mouth. At operation, a cleft palate and a rudimentary tongue were also found. Death from gangrenous stomatitis followed shortly.

EMERSON, Boston.

Diseases of the New-Born

CEREBRAL BIRTH HEMORRHAGE IN PREMATURE AND IMMATURE INFANTS. AARON CAPPER, Am. J. Obst. & Gynec. **17**:106 (July) 1929.

The author makes a definite distinction between a premature and an immature infant. He defines a premature infant as one born before term, while he classifies as immature those infants born at term whose birth weight is under 5 pounds (2,267.9 Gm.)

The immature as well as the premature infants show a marked insufficiency of the elastic supporting tissues in the vascular system which probably accounts for the increased tendency to hemorrhage. These hemorrhages may be intracranial, subcutaneous or in other important organs. Especial care must therefore be exercised in the delivery and resuscitation of these children.

The usual lumbar puncture and intramuscular injections of blood are used in the treatment for the intracranial types of hemorrhage. Cisternal and ventricular puncture are reserved for the patients who do not respond to the usual treatment.

ALLEN, Chicago.

EPIDEMIC PEMPHIGUS NEONATORUM: A METHOD OF TREATMENT. J. ARTHUR KEHO, Northwest. Med. **28**:37 (Jan.) 1929.

This disease, frequent in the nurseries of maternity hospitals, manifests itself as vesicles, the lymph of which contains a gram-positive diplococcus, growing as a staphylococcus on ordinary mediums. If untreated, the vesicles spread to other parts of the infants' skin and to that of other infants. The disease is fairly resistant to treatment with ammoniated mercury, mercurochrome-220 soluble, gentian violet, tar and ultraviolet light; it is susceptible to copper. Keho believes that the organism is contained in the vaginal discharge of a few mothers. His method of treatment is the use of an ointment of 1 per cent copper oleate in lard or olive oil. After the use of this ointment on infected infants, the lesions promptly cleared. The use of the ointment to remove the vernix caseosa in a series of newborn infants prevented the development of a lesion, though they were exposed to the other infected patients.

SCOTT, Philadelphia.

SOME TYPES OF INFECTION IN THE NEWLY BORN. HECTOR CHARLES CAMERON, Lancet **1**:1127 (June 1) 1929.

An estimate of the efficiency of the circulatory, respiratory and suction apparatus of a child serves directly as a measure of its well being and vitality. Of these, the infant's power of suction is the most useful index.

The high neonatal mortality (of 82.9 deaths per thousand live births, more than half occurred during the first month) is due to: (*a*) developmental defects incompatible with life; (*b*) gross prematurity which also predisposes to (*c*) sepsis neonatorum and other infections, (*d*) functional weakness of particular organs, jaundice, the hemorrhagic disorder, disorders of gastric and intestinal peristalsis, and (*e*) birth trauma.

Septic infection as it occurs in the newly born has the following peculiarities: Generalization of the infection often takes place without visible involvement of the lymphatics and without enlargement of the lymphatic glands. There is a predominance of toxic symptoms over infective: coma, convulsions, muscular rigidity, diarrhea and diffuse hemorrhages.

Increased susceptibility of the newly born to septic infection is due in part to the structural peculiarities of the skin and mucous membranes which render them much more readily permeable to bacteria and also to a deficiency of antibodies in the blood, increased by the abandonment of breast feeding.

Often the umbilical wound is the primary source of infection, but close observation will also show that the infection of the umbilicus is often secondary to generalized infection. Rivaling the umbilicus as a portal of infection are all eczematous and intertriginous erosions of the skin.

In general, opinion inclines to the view that the frequent intestinal symptoms are secondary results of infection.

Clinical varieties of sepsis neonatorum differ according to the system that happens to bear the brunt of the attack, e. g., the pulmonary, gastro-intestinal, cerebrospinal and cutaneous forms.

Trismus neonatorum is in general a manifestation, not of tetanus proper, but of sepsis; there is no justification for considering the two conditions identical. In almost all cases of sepsis neonatorum some evidence will be found of excessive rigidity of the muscles. In the variety of sepsis neonatorum here considered, this rigidity of the muscles is the most characteristic feature and is developed to a remarkable extent. The rigidity of the jaw is in keeping with the rigidity of all the muscles. In patients who recover, the spasm of the jaw disappears comparatively early.

LANGMANN, New York.

STUDIES IN HEIGHT, WEIGHT AND SITTING HEIGHT OF NEW-BORN INFANTS. H. SLOBOSIANO and P. HERSCOVICI, Nourrisson **17**:133 (May) 1929.

These studies are based on the formulas elaborated by Pirquet. The gewicht-linear or geli (i. e., the cube root of the weight multiplied by 10) parallels the sitting height and varies from 17 to 22 at the sixth month of fetal life to from 29 to 35 at term.

The length of the legs is 12 or 13 cm. at six months and is increased to from 16 to 21 cm. at term.

The sitting height is 23 or 24 cm. at six months and from 30 to 34 cm. at term.

The gelidusi (the cube root of 10 times the weight divided by the sitting height) is low in the six month fetus, from 96 to 100, increasing to from 101 to 104 in the fetus born at term.

MCCLELLAND, Cleveland.

CONVULSIONS IN THE NEW-BORN INFANT. R. WAITZ, Rev. franç. de Pédiat. **5**: 171 (April) 1929.

In a series of 1,471 new-born infants, the author encountered 19 cases of motor disturbances. One showed a slight contracture with hypertonicity lasting for forty-eight hours; the other 18 showed either clonic or tonic convulsions. The convulsions occurred most frequently from the second to the fourth day. Associated symptoms were cyanosis, bulging of the fontanel and thermic instability. Etiologically, all cases were associated with difficult labor, prematurity or twin births. Abundant fluid was obtained on lumbar puncture in 89 per cent of the

cases. The author considers this in itself pathologic, believing that in the normal new-born infant no fluid is obtained. Further, the fluid showed increased amounts of albumin and cells of the reticular or endothelial type. This the author considers characteristic of acute edema of the meninges. Five cases which came to autopsy showed such an edema, designated by the author, aseptic meningitis. One concludes, then, that mechanical factors are responsible for convulsions in the new-born infant, and that every precaution should be taken to avoid difficult or premature labor.

LESLIE, Evanston, Ill.

THE FIRST APPLICATION OF THE NEW-BORN INFANT TO THE BREAST. W. REIPRICH, Deutsche med. Wchnschr. **55**:595 (June 7) 1929.

Referring to the attitude of the obstetrician and of the pediatrician as to the proper time after delivery at which to put the infant to the breast for the first time and asserting that both of these views are more or less empiric, the author cities the investigations of Engelmann and Hamburger and the later work of Willkomm. Both of these definitely favor the longer period of starvation. Reiprich's work was done on 400 new-born infants. From this group he excluded all premature and congenitally weak infants. The purpose of the investigation was to determine (1) the amount of milk obtained at the first nursing, (2) the amount obtained during the first twenty-four hours of nursing, (3) the amount obtained during the first three days, (4) the effect on the initial loss of weight and (5) the gain at the end of ten days.

Two hundred of the infants were put to breast for the first time from twelve to twenty hours after delivery, and the other 200 were not given the breast until from twenty-four to thirty hours had elapsed. From this series, Reiprich finds: 1. In the first group (twelve to twenty hours) the amount of food received from the breast was 5 cc., in the second group, 20 cc. 2. The amount during the first day was 95 cc. for the twelve to twenty hour group, and twice as much (180 cc.) for the twenty-four to thirty hour group. 3. The three day quantity was practically 50 per cent greater in the twenty-four to thirty hour group. 4. The initial loss of weight was practically the same in both groups. 5. Twenty-five per cent of the infants in the twelve to twenty hour group had regained the birth weight by the tenth day, while 33 per cent showed the same gain in the other group.

SCHERER, Duluth, Minn.

LINES IN THE FACE OF THE NEW-BORN INFANT. RUDOLPH FISCHL, Monatschr. f. Kinderh. **43**:411 (June) 1929.

There seems to be a general opinion that the face of the new-born infant is unfurrowed and masklike. In a study of a great number of new-born infants, Fischl finds that certain fissures occur with relative frequency. The first and most common resembles the dent made by the nose piece of a pair of spectacles. The second is a set of fine lines running from the inner angle of the eye upward over the glabella. The third and least frequent are the lines in the forehead which occur in the adult when he is anxious and worried.

GERSTLEY, Chicago.

THE EFFECT ON THE NEW-BORN INFANT OF IRRADIATING THE MOTHER DURING PREGNANCY. W. FREUND and K. SCHMITT, Monatschr. f. Kinderh. **43**:424 (June) 1929.

Two hundred and twenty-nine women were given irradiation of ultraviolet light during their pregnancy. The treatments started at two minutes and were increased to a duration of twenty minutes. The total periods varied from one-half to twelve hours. Two hundred and twenty-two women were used as controls. The new-born infants of the group receiving irradiations averaged 0.6 cm. more in length and 155 Gm. more in weight than those from the groups used as controls.

The differences were not marked, but seemed to be more outspoken in the children born in the winter than in those born in the summer. In the appearance of rickets and in the blood phosphorus, there was a slight balance in favor of those receiving irradiations.

GERSTLEY, Chicago.

Acute Infections

EXTENSIVE, DIFFUSE, HYDROPIC DEGENERATION OF THE MYOCARDIUM, ASSOCIATED WITH A DIPHTHERITIC INFECTION. B. ROMAN, Bull. Buffalo Gen. Hosp. **8**:29 (June) 1929.

A child, aged 4 months, had undergone an unsuccessful attempt to repair a harelip and a cleft palate when he was 2 months of age. He now entered the hospital because of furunculosis. A throat culture showed *Bacillus diphtheriae,* and antitoxin was given. The temperature did not rise above 101.4 F, but the child died forty-eight hours later. The diagnosis at autopsy was high grade hypertrophy and degeneration of the heart, with edema of the brain and the lungs. Microscopic sections of the heart showed widespread liquefaction of the myocardial fibers.

SANFORD, Chicago.

CLINICAL RESULTS WITH MEASLES STREPTOCOCCUS TOXIN AND ANTITOXIN. N. S. FERRY AND OTHERS, J. A. M. A. **91**:1277 (Oct. 27) 1928.

The average actual protection computed in three series of cases in three different institutions, following the use of measles streptococcus, was 66 per cent. At two institutions, in which the dose of antitoxin was 20 instead of 10 cc., the average protection was 78 per cent. This was apparently far superior to the computed actual protection following the use of measles convalescent serum.

BONAR, Salt Lake City.

PAROXYSMAL SNEEZING AS AN EQUIVALENT OF THE PAROXYSMAL COUGH OF PERTUSSIS. H. S. REICHLE, J. A. M. A. **92**:443 (Feb. 9) 1929.

Paroxysmal sneezing may be a valuable diagnostic aid in the early diagnosis of pertussis, and in young children may partially or entirely supplant the cough. The attacks are typically convulsive, with congestion of the head, cyanosis and exhaustion, and often expulsion of the usual tenacious mucus. They may be accompanied by coryza, an inspiratory crow and vomiting.

BONAR, Salt Lake City.

ACUTE GLANDULAR FEVER OF PFEIFFER. CLARA M. DAVIS, J. A. M. A. **92**:1417 (April 27) 1929.

An epidemic of acute glandular fever occurred in a small nursery. All the infants and one nursemaid were affected to a varying degree of severity. The spleen was palpable in only one case. Lymphocytosis occurred early in the incubation period, which in one well controlled instance occurred eleven days after exposure. Relapses were common. Suppurative complications occurred only in infants with mixed infections. The infants recovered from the illness in from three to six days, and the swollen glands returned to normal within four weeks. No bacteriologic study was reported.

BONAR, Salt Lake City.

THE HEALTHY CARRIER IN SCARLET FEVER. RUTH TUNNICLIFF and T. T. CROOKS, J. A. M. A. **92**:1498 (May 4) 1929.

The source of several cases of scarlet fever in a children's ward was traced to scarlet fever streptococci found in a healthy attendant's throat. After removal of the tonsils, hemolytic streptococci disappeared and no more cases of scarlet fever

developed. A short time later, a similar experience occurred. In all, fourteen cases of scarlet fever were traced to three healthy carriers of scarlet fever streptococci. By a rapid and simple method described, it is possible to detect carriers without difficulty.

BONAR, Salt Lake City.

HYPERSENSITIVENESS TO DIPHTHERIA BACILLI. JAMES M. NEILL and WILLIAM L. FLEMING, J. Exper. Med. **49**:33, 1929.

The paper describes an "immediate" skin reaction to derivatives of the diphtheria bacillus which is shown to be distinct from the "delayed" or "pseudoreaction" commonly seen in Schick tests on adults. The "immediate" reaction was passively transferred to local areas of the skin of other people.

[ARCH. PATH.]

A STATISTICAL STUDY OF SCARLET FEVER AND DIPHTHERIA. HILDA M. WOODS, J. Hyg. **28**:147, 1928.

The mortality from scarlet fever has declined relatively the most at the ages between 0 and 5 years, and there is a tendency for a greater proportion of the mortality to occur among older children and young adults.

The mortality from diphtheria appears to be concentrated on children of the early school age and decreased at older ages.

The decline in incidence and mortality from scarlet fever has been as great in towns with little isolation as in those in which the majority of patients are hospitalized.

It cannot be shown that during the period studied isolation has had either a good or bad effect on the prevalence or mortality of scarlet fever.

As far as the analysis goes and the method of correlation can show, there is no evidence pointing to the advantageous results of the isolation of patients with diphtheria in London.

[ARCH. PATH.]

ANALYSIS OF THE MORTALITY FIGURES OF THE WILLARD PARKER HOSPITAL FOR THE YEARS 1922-1927, INCLUSIVE. SHIRLEY W. WYNNE, New York State J. Med. **29**:12 (Jan. 1) 1929.

Since the reorganization of the Health Department hospitals in New York City in 1923, the general mortality at Willard Parker Hospital has been reduced from 16.7 to 7.3, a reduction of 56.3 per cent. The mortality from diphtheria fell from 18.1 to 8.1 per cent. This improvement is largely attributed to the use of suction in laryngeal diphtheria. In 1922, 234 patients, or 14.2 per cent of those treated, were intubated. In 1927, only 72 patients, or 4.5 per cent, were intubated. The fatality rate among those intubated has also fallen from 54 to 16.6 per cent. In the last three years, cases that required prolonged use of the tracheal tube have developed, and 54 patients with this type of case who have been living in the hospitals since 1923 have been returned to their homes cured. Measles is attended by the highest mortality of all the more common contagious diseases, but the fatality rate of 22.4 in 1922 fell to 10.4 in 1926, and to 9.5 in 1927. The death rate for scarlet fever has been reduced from 8.3 to 2.3 per cent, largely owing to the use of serum in severe cases.

AIKMAN, Rochester, N.Y.

THE RELATION OF ALLERGY TO SCARLET FEVER. FRANKLIN A. STEVENS and A. R. DOCHEZ, New York State J. Med. **29**:22 (Jan. 1) 1929.

It was at first thought that *Streptococcus hemolyticus*, like the diphtheria bacillus, produced, a true toxin. It is now believed that there are too many discrepancies for this theory to hold. Clinical observations and laboratory experiments show that the toxic substance is not a toxin but an allergin or toxallergin and that the symptoms are allergic. Three periods occur in the life of man. The first period is before the child has become sensitized to the streptococcus, the

cutaneous reaction being negative and the child not susceptible to the rash of scarlatina. In the second period, the child has become sensitive to the streptococcus, gives a positive cutaneous reaction and can have the disease. The third period is reached after repeated infections with the streptococcus, as from sore throat or scarlet fever; then antitoxin appears in the blood, the cutaneous reaction is negative and the person is immune.

AIKMAN, Rochester, N.Y.

POLIOMYELITIS IN SYRACUSE. A. CLEMENT SILVERMAN, New York State J. Med. **29**:145 (Feb. 1) 1929.

From 1921 to 1927, inclusive, 299 cases of poliomyelitis occurred in Syracuse, with 41 deaths. In the 1916 epidemic, Syracuse, with a population of 160,000, reported 229 cases and 64 deaths. From 1916 to 1921, only 7 cases and 2 deaths were reported.

In 1924, 152 cases occurred when Syracuse and the four counties bordering it had 50 per cent of the total number of cases of poliomyelitis reported in New York State. Three epidemics have occurred in the last seven years. Suspects were examined by diagnosticians from the health bureau, and if the cell count and globulin in the spinal fluid were positive, convalescent serum was injected intraspinally. This was repeated in from twelve to twenty-four hours if necessary. Cell counts as low as 25 were found in patients subsequently showing paralysis.

From the results obtained, the author believes that "immune serum treatment is the logical one to use."

AIKMAN, Rochester, N. Y.

ACUTE RHEUMATISM IN CHILDHOOD AND ITS SEQUELAE. E. B. STERLING, Pub. Health Rep. **44**:1488 (June 21) 1929.

Since disease of the heart in childhood results so frequently in a damaged heart, it is a distinct public health problem, irrespective of its actual effect on the death rate. The child with disease of the heart is handicapped, and handicapped persons are likely to become problems in the community. The establishment of "cardiac classes" in schools is one form of the community's partial soluion of this problem. Any reduction in the incidence of acute rheumatic fever is an important contribution to the public health.

SANFORD, Chicago.

COMPLETENESS OF REPORTING OF MEASLES, WHOOPING COUGH AND CHICKEN POX AT DIFFERENT AGES. E. SYDENSTRICKER, Pub. Health Rep. **44**:1537 (June 28) 1929.

In a continuation of the studies of morbidity in Hagerstown, Md., it was found that the greater incompleteness of reports on children of preschool age is due to the fact that fewer children in this group are seen by physicians. This results in an incompleteness in morbidity tables for various ages, and should be taken into consideration when statistics are sought in these tables.

SANFORD, Chicago.

REPORT OF THE ROYAL COMMISSION OF INQUIRY INTO FATALITIES FROM TOXIN-ANTITOXIN AT BUNDABERG. CANBERRA, M. J. Australia **2**:2 and 38, 1928.

Of twenty-one children injected with toxin-antitoxin on Jan. 27, 1928, some with the initial and some with the second dose, eighteen became ill and twelve died. The same bottle had been used several times previously without untoward effects. The symptoms were similar in all the fatal cases, beginning from five to eight hours after injection with vomiting and diarrhea, fever, rapid pulse, cyanosis and circulatory failure. The deaths occurred in from fifteen to thirty-four hours. The survivors developed abscesses at the site of inoculation. The most significant postmortem observation was degenerative change of the lymphoid tissue throughout, suggestive of the action of a toxic agent in the blood stream. Changes peculiar to the action of diphtheria toxin, such as fatty degeneration

of the heart muscle or hemorrhages, were not found. Examination of the remaining toxin-antitoxin mixture showed it to be cloudy on the following day, and staphylococci were cultivated both from it and from the abscesses. No evidence of tetanus or of free toxin was found in the mixture, and injections of antitoxin in the sick children had no effect. The symptoms and pathologic observations pointed to a staphylococcus infection as the most likely cause of the illnesses, in spite of the rapidity of the deaths and absence of metastatic abscesses in the survivors. The organism was not highly pathogenic for laboratory animals, except for the rabbit. Skin tests in human beings with a filtrate produced marked reactions in some persons and none in others, suggesting a possible explanation of the failure of some of the children to react.

The batch of toxin-antitoxin in question was issued without addition of a preservative, and the bottle was kept at room temperature, so that conditions were favorable for the multiplication of organisms. There were two possible sources of contamination. The needles used for the injections were lifted out of sterile water with the fingers instead of with forceps, and air was necessarily injected onto the rubber-capped bottle as the fluid was removed. Although the fingers of the operator appeared to be the most likely source of the staphylococci in this case, an experiment was made to investigate the latter possibility. Air was injected and fluid removed with sterile needles in the usual manner from a number of rubber-capped bottles of toxin-antitoxin without antiseptic, and 30 per cent of them were found to be contaminated in this way. No contamination occurred in the presence of an antiseptic.

The commission concluded that the deaths were due to staphylococci with which the mixture was contaminated during the first injections made from the bottle, and that the repeated use of material from a rubber-capped bottle containing no antiseptic is dangerous. It recommended that biologic products in which growth is possible should not be issued in this form, and that all products not containing an antiseptic should be so labelled, with the warning that they must be completely used at one time or the remainder discarded. Special training for those engaging in the immunization branch of public health work was advised.

BEATRICE R. LOVETT.

PNEUMOCOCCEMIA WITH MULTIPLE MANIFESTATIONS. JOSE BONANA and ROGELIO CHARLONE, Arch. latino-am. de pediat. **23**:69 (Feb.) 1929.

Pneumococcemia was observed in epidemic form. The case of a child, aged 6 years, is reported as illustrating how this condition may cause a serious and extensive involvement of the whole organism. The patient developed double pneumonia with bilateral pleurisy, acute nephritis, a cardiac complication and meningeal and abdominal symptoms. The case ended fatally in spite of the child's partial recovery from some of the more severe complications.

ENCEPHALITIS IN PERTUSSIS. VICTOR ZERBINO, Arch. latino-am. de pediat. **23**:95 (Feb.) 1929.

An infant, aged 2 years, rather suddenly and early during the course of pertussis developed repeated attacks of spasm of the glottis accompanied by pronounced attacks of asphyxia and some hyperpyrexia.

Respiration was irregular during and following these attacks, and there were numerous symptoms of involvement of the central nervous system. Death occurred on the tenth day following the development of the symptoms.

SCHLUTZ, Minneapolis.

PNEUMOCOCCEMIA IN A CHILD, AGED FOUR YEARS. F. HURTADO, Bol. Soc. Cubana de pediat. **3**:128 (March) 1929.

Hurtado presents a case of a child, aged 4½ years, who developed empyema and a pleural involvement following pneumonia due to type III pneumococcus.

MENINGOCOCCUS INFECTION IN INFANTS. C. GIAUME, Riv. di clin. pediat. **27:** 351 (May) 1929.

The author discusses the different manifestations of meningococcus infection in infants. Early symptoms permit the division into such types as: gastro-intestinal, respiratory, tetanoid, purpuric, articular and monosymptomatic (rigid neck).

HIGGINS, Boston.

MALARIAL TREATMENT IN GONORRHEAL VULVOVAGINITIS. W. COURTIN, Arch. f. Kinderh. **86:**28 (Dec. 28) 1928.

During the past year in Ibrahim's clinic, three children, from 4 to 7 years of age, were given this treatment. It consisted of an intravenous injection of from 5 to 6 cm. of malarial blood, giving a negative Wassermann reaction. Local treatment was carried on with a strong silver protein solution, 1 per cent in the urethra and 2 per cent in the vagina. The systemic reaction came between the ninth and fourteenth days. If the temperature exceeded 40 C. (104 F.), 1 cc. of metrazol was given prophylactically. On the day following the fifteenth rise in temperature, 0.3 Gm. of neoarsphenamine was given. Courtin states his belief that this form of treatment is indicated if there is no improvement after from six to eight weeks of local treatment, and the child has no pathologic cardiac condition or tuberculosis.

SANFORD, Chicago.

THE SENSITIVENESS OF CHILDREN WITH MEASLES AND SCARLET FEVER TO CUTANEOUS INJECTIONS OF EPINEPHRINE. M. RUEFF, Arch. f. Kinderh. **86:**37 (Dec. 28) 1928.

Using Müller's capillary microscopic method of studying epinephrine blanching, Rueff found the reaction time in 370 normal children to be between fourteen and twenty-one seconds. In 21 cases of measles, the time averaged thirty-six seconds on the first day and fell to twenty-four seconds by the fourth day. The reduction in time was then slower until it reached eighteen seconds on the twenty-first day. In 13 cases of scarlet fever, the time averaged twenty-seven seconds on the first day and fell to normal limits by the third. It was below normal, or twelve seconds, on the sixth day and remained below thereafter. In several cases of serum exanthems, the time remained below normal throughout the entire period.

SANFORD, Chicago.

GENERALIZED EMPHYSEMA IN BRONCHOPNEUMONIA AND WHOOPING COUGH. H. UNGER, Arch. f. Kinderh. **86:**281 (March 28) 1929.

Unger reports a fatal case of bronchopneumonia and whooping cough in an infant, aged 10 months. At necropsy there were found cutaneous emphysema in the right supraclavicular region, bullous emphysema of both lungs, and interstitial emphysema with the formation of large bubbles of air in the connective tissue of the hilum of the lung and of the entire mediastinum.

VALUE OF VON KÉSMÁRSZKY'S METHOD OF IMMUNIZATION AGAINST CHICKENPOX. A. BÄUMLER, Arch. f. Kinderh. **86:**309 (March 28) 1929.

From his experience in the immunization of ninety-nine children, Bäumler states that von Késmárszky's method of active, intracutaneous immunization against chickenpox is of little value.

SANFORD, Chicago.

HEMOLYTIC STREPTOCOCCI IN HEALTHY PERSONS AND THEIR IMPORTANCE IN THE PREVENTION OF SCARLET FEVER. K. MEYER and W. LOWENBERG, Med. Klin. **25:**107 (Jan. 18) 1929.

In connection with an epidemic of scarlet fever in their wards, the authors examined fifty-nine physicians and nurses working in the wards. From forty-one

of these, i. e., from 69 per cent, hemolytic streptococci were obtained on culture. The personnel of the kitchen was also examined; hemolytic streptococci were found in thirty of fifty-seven persons, i. e., in 52.6 per cent. Newly admitted patients who did not show any infectious diseases showed about the same frequency of positive observations. In children, particularly infants, hemolytic streptococci were found much less frequently. The authors think that hemolytic streptococci are found quite frequently in the throat of healthy persons. The organisms could almost be called ubiquitous. The bacteriologic diagnosis of hemolytic streptococci is rather difficult. Concerted efforts seem to be desirable to work out reliable methods for determining hemolysis and for making a more satisfactory diagnosis. Only after an extensive work of this type can conclusions be drawn as to the importance of hemolytic streptococci in the etiology of scarlet fever.

ZENTAY, St. Louis.

PROPHYLAXIS AND THERAPY IN WHOOPING COUGH. W. HOFFMANN, Monatschr. f. Kinderh. **43**:41 (March) 1929.

In an epidemic of whooping cough in his institution, the author attempted to immunize the uninfected children with a vaccine containing the Bordet bacilli, as well as the influenza and pneumonia organisms. He does not mention how many of these children developed the disease and how many were protected. Three months later, however, whooping cough again appeared, and all of the previously inoculated children developed the infection.

On the other hand, he is entirely convinced that a mixed whooping cough vaccine containing the same organisms in different quantities, was of great value in the actual treatment for the disease. He also obtained good results with the vaccine put up by some of the German firms. In addition to this treatment, he used intramuscular injections of ether every other day in doses of from 0.5 to 2.0 cc., depending on the age of the child. As ether given intramuscularly is prone to cause a necrosis, he suggests as a substitute from 1 to 2 cc. of ether in 15 cc. of olive oil, as recommended by Goldbloom, to be used as an enema twice a day.

GERSTLEY, Chicago.

THE HISTOLOGIC CHANGES OF THE THYMUS GLAND IN CHILDREN WITH SCARLET FEVER. P. W. SSIPOWSKY, Frankfurt. Ztschr. f. Path. **36**:123, 1928.

The weight of the thymus gland was found to be less than normal in a series of twenty-nine children who had had scarlet fever. This loss of weight was due to a disappearance of the lymphocytes, an effect of the toxin. The lobules of the organ thus lose their typical differentiation. The medullar and cortical portion of the thymus gland both show a predominance of the reticulo-epithelial structure. There is even a proliferation of the latter formations, so that macrophage-like cells are found which are filled with fat. The picture of these changes is therefore similar to those described for other acute infectious diseases such as dysentery or diphtheria.

JEAN OLIVER.

ACTIVE IMMUNIZATION AGAINST DIPHTHERIA WITH TOXOID. DORA HARTMANN-KARPLUS, Wien. klin. Wchnschr. **42**:706 (May 23) 1929.

The author used a toxoid prepared in Vienna. The quantity injected was made up to 2 cc. with salt solution. In group 1, twenty-five children convalescent from scarlet fever received 0.5, 1 and 1 cc. at weekly intervals. After five weeks, 88 per cent gave negative reactions to the Schick test, seventeen gave practically no reactions, seven had a moderate reaction and one a severe reaction. In group 2, twenty-five children convalescent from scarlet fever received 0.2, 0.2 and 0.2 cc. at intervals of three days. After five weeks, 68 per cent gave negative reactions to the Schick test. None had more than a slight reaction. In group 3, twenty-five children convalescent from scarlet fever received 0.5, 0.5 and 0.5 cc. at intervals of

three days. After five weeks, 68 per cent gave negative reactions to the Schick test, twenty-one had little reaction, three a moderate reaction and one a severe reaction. In group 4, twenty-five children in the medical division received five injections of 0.2 cc. at intervals of four days. After five weeks, 92 per cent gave negative reactions to the Schick test. Twenty had little or no reaction, five had a moderate reaction and none a severe reaction.

It is well known that patients convalescing from scarlet fever are difficult to immunize. Fifty-six per cent of the children were over 6 years of age, but 94 per cent of the reactions occurred in children over 6. The children who gave a combined positive reaction on the original Schick test reacted more severely on immunization. The two most severe reactions occurred in children aged 6½ and 7 years. The author questions the practicability of five injections in routine work, and feels that immunization with the smaller total quantities of toxoid may not be lasting.

CLAUSEN, Rochester, N. Y.

THE FERMENTATIVE METHOD OF PRODUCING DIPHTHERIA TOXIN IN VITRO. W. M. SDRAWOSMISSLOW and N. E. KOSTROMIN, Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:1, 1927.

The authors believe that antibodies result from a molecular ungrouping of a combination of antigen and ferment. Trypsin mixed with diphtheria toxin in vitro resulted in an antiserum which had antitoxic properties. They consider that in infection the balance between the production of ferments and the antiferment action of the antigen determines the final result, all antibodies being merely changed ferments.

PAUL R. CANNON.

FURTHER INVESTIGATIONS OF THE INHERITABILITY OF SUSCEPTIBILITY TO INFECTIOUS DISEASES. H. HIRSZFELDT and L. HIRSZFELDT, Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:81, 1927.

Schick tests in 116 families and Dick tests in 55 families showed that when both parents gave positive reactions, most of the children gave positive reactions, whereas when both parents gave negative reactions, approximately two thirds of the children reacted negatively and one third positively. When one parent gave a negative reaction and the other a positive one, about one half of the children gave a positive reaction. The authors then discuss the theoretical aspects of these observations.

PAUL R. CANNON.

THE INFLUENCE OF CERTAIN AMINO-ACIDS ON CULTURES OF DIPHTHERIA BACILLI. B. SBARSKY and Z. JERMOLJEWA, Ztschr. f. Immunitätsforsch. u. exper. Therap. **54**:105, 1927.

In a previous paper, Sbarsky and Subkowa (*Biochem. Ztschr.*, 1925, p. 161), showed that amino-acids, particularly tyrosine, inactivated diphtheria toxin. The present authors report the effect on diphtheria bacilli. Small amounts of amino-acids in cultures do not kill the bacteria themselves, but tyrosine diminishes the toxicity of mildly toxicogenic cultures of diphtheria bacilli when injected subcutaneously. The effect is minimal, however, with toxic strains. Alanine, leucine and glycocol have no such effect. Tyrosine in 0.5 per cent concentration in broth cultures diminishes the production of toxin from ten to twenty times.

PAUL R. CANNON.

VARIOLA-VACCINIA. HANS DEMME, Ztschr. f. Immunitätsforsch. u. exper. Therap. **55**:191, 1928.

The problem of neurotropism of the variola-vaccinia virus was investigated. Inoculations were made into the cornea, skin, testicle, sciatic nerve and subdural space of rabbits. Encephalitis was absent in all rabbits inoculated in peripheral

organs. Pleocytosis of the spinal fluid following inoculation was interpreted as evidence of the participation of the central nervous system in the defensive reaction of the organism. There was no indication that the virus wanders by way of the nerves; on the contrary, the fact that the clinical course was the same after inoculation into the sciatic nerve, with and without previous surgical interruption, and the occurrence of cases of general vaccinia after inoculation of this nerve and the cornea point to the carriage of the virus by the blood. The encephalitis occurring after intracerebral inoculation was a nonspecific inflammatory reaction restricted to the meninges and vascular sheaths (mesenchymatous reaction) without participation of the ectodermal nervous substance. As these results differ from those after inoculation of herpes virus, variola-vaccinia does not belong to the neurotropic ectodermatoses. Its close relationship to herpes is denied. The vaccinia infection is interpreted as a general infection. It may activate a virus already present in the body or prepare the field for its activity. This interpretation applies also to human postvaccinial encephalitis.

WILLIAM C. HUEPER.

ACUTE EPIDEMIC INFANTILE PARALYSIS (HEINE-MEDIN) IN EAST PRUSSIA. RUTH LINDSTÄDT, Ztschr. f. Kinderh. **47**:372 (March 23) 1929.

Lindstädt reports her observations on an epidemic of infantile paralysis in East Prussia from May, 1926, to April, 1928; there were 177 cases in all, several of which are of great interest: (1) a purely cerebral case with an encephalitic process leading to spastic hemiplegia, in which the spinal fluid was normal; (2) a case with an acute onset of blindness, which gradually improved in six weeks, in which there was general diminution of muscle tone with flaccid paralysis in only the anterior muscles of the neck; the acute onset and the course justified the assumption that the bilateral disease of the optic nerves was due to the etiologic agent of Flexner-Noguchi, although the localization was unusual; (3) a case in which two false diagnoses were first made of appendicitis and tuberculous meningitis, respectively. Concerning the cases as a whole, a tendency toward a second peak of great incidence, pointed out by Aycock, could not be confirmed. On the contrary, March and April, the months designated by him, as showing a renewed period of activity, were to be looked on as quiet months. Likewise divergent was the observation of a remarkably constant but small peak in January, a month usually considered the quietest. An explanation of the shifting of the quiet period forward by four months is to be found, perhaps, in the difference in the influence of the weather which exists between America and Western Europe, on the one hand, and the Eastern Provinces of Germany, on the other.

In general, there was a distinct preponderance of characteristic poliomyelitis and of the spinal localization of the disease process. Only eight of thirty-two cases could be assigned to special groups; two cases belonged to the purely cerebral type, three to the bulbopontile type and three to the neuritic type with a focus in the spinal cord as well. The history in only two cases indicated the abortive type; unfortunately, none came under observation. This does not correspond to Wickman's grouping of meningitic cases and cases giving the picture of Landry's disease. The latter semed to be better classified under the spinal form. Meningitic changes again are pathologico-anatomically regular cosymptoms in the beginning of acute infantile paralysis, although they often do not come to light clinically. Two cases of marked meningitic character were to be grouped according to the paralysis occurring: bulbopontile and poliomyelitic. Purely serous meningitis, without other accompanying symptoms that point to an infantile infection the etiology of which could be explained only by the demonstration of direct contact with the virus, should be looked on as abortive cases just as those which show only manifest angina. On the basis of Lindstädt's observations from the pathologico-anatomic point of view, the cases could be divided into five groups: (1) spinal (poliomyelitic), (2) bulbopontile, (3) cerebral (encephalitic), (4) neuritic and (5) abortive. Because of the many sided picture of the disease, the present designation of

anterior poliomyelitis, which includes only a narrow even if the largest subgroup, ought no longer to be considered correct. A better name would be acute epidemic infantile paralysis.

EMERSON, Boston.

THE DICK REACTION AND SMALLPOX VACCINATION. L. O. FINKELSTEIN and R. A. WILFAND, Ztschr. f. Kinderh. **47**:417 (March 23) 1929.

Inoculation against smallpox doubtless acted on the outcome of the Dick test, because a previous negative reaction was transformed to a positive reaction. This was especially definite after intracutaneous smallpox inoculation of smallpox lymph and Dick toxin, but could be established after the usual inoculation with cowpox. The positive Dick reaction appeared on about the sixteenth day after the inoculation with cowpox, and lasted for several months. In consideration of the fact that, under the conditions described, definite positive reactions (negative reactions in the controls) were always obtained, that the Dick reaction remained negative in repeated tests and that the Dick antiscarlet fever serum again transformed a positive Dick reaction to a negative reaction, the investigators would like to consider these reactions as genuine. The hypothesis of Moro on parallergy can be extended to the opposite condition between cowpox inoculation and the Dick reaction.

EMERSON, Boston.

THE BEHAVIOR OF WHITE BLOOD CORPUSCLES IN MEASLES. Z. OLECHNOWIZOWNA, Pediatria Polska **9**:21 (Jan. and Feb.) 1929.

Thirty-two cases of measles were studied. Blood was taken when the stomach was empty, and in infants three hours after feeding. The author used Schilling's method, and the following results were obtained: 1. In the period of incubation, most cases presented "leukocytosis and, frequently, eosinophilia. 2. In the period of eruption, mild cases showed leukopenia. In severe cases, leukocytosis, lymphocytosis and the absence of monocytes were observed. 3. In the period of convalescence, there was a normal leukocytosis, a normal lymphocytosis and a return to normal of the monocytes and other cells. These conditions rarely vary, and only in children up to 4 years of age.

KRUPNISKI, Chicago.

IMMUNIZATION EXPERIMENTS IN AN EPIDEMIC OF MUMPS. J. KRAMAR and J. BARLA-SZABO, Orvosi hetil. **73**:601 (June 22) 1929.

In a boarding school for boys, a severe epidemic of mumps broke out. After about six days, the experiments in active immunization were started. Citrated blood of a boy, aged 14 years, who had a rather severe case of mumps, was used; 0.1 cc. was injected intracutaneously. Injections were given to 112 children, and 18 were left as a control group. When the cases that occurred the first week after the immunization were excluded, the immunized group showed an incidence of 7.9 per cent and the unimmunized group, an incidence of 35.5 per cent. The authors think that active immunization with their method is advisable in closed institutions. The method is without any untoward effects.

ZENTAY, St. Louis.

PATHOLOGIC SIGNIFICANCE OF THE INCREASE IN BLOOD AMMONIA DURING CONVULSIONS IN DYSENTERY. H. HARA, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 1.

The author proceeds with his study on the assumption that the convulsive attacks so often encountered in the course of acute infections of the gastrointestinal tract in infancy and early childhood, especially during the course of severe dysentery, are the manifestations of intoxication due to an increased amount of some intermediary products of metabolism, an increase far surpassing the degree of detoxication which normally occurs. His conclusions are as follows: 1. In acute gastro-enteritis, even in cases showing a mild organic pathologic condition,

there is an acceleration of permeability through the mucosa, the degree of permeability being in direct proportion to the severity of intoxication. 2. During the convulsive attacks in the course of severe dysentery, the amount of blood ammonia increases from seven to eleven times as compared with the normal value. In rabbits the same increase (from five and one-half to eleven times) of blood ammonia can be demonstrated during the convulsive attacks. This increase is singularly absent in other types of convulsions in infants, and the same is true in rabbits during convulsions elicited by means of picrotoxin or strychnine. Again, there is no increase of guanidine and methyl guanidine in the urine of infants collected during the convulsive attacks in severe dysentery. It appears, therefore, that convulsive attacks in severe dysentery and the increase in blood ammonia have causative relations to each other, as the increase in ammonia is not the result of any damage to the central nervous system. 3. In infantile dysentery, especially in its severe form, there is a noted functional disturbance in the formation of urea by the liver, a retardation of phagocytosis in the reticulo-endothelial cells, a prolongation of the elimination of dye, an appearance of acetone, urobilin, urobilinogen and bilirubin in the urine, and a slight increase in serum bilirubin. 4. The pathologic changes of the liver in infantile dysentery and dysentery produced experimentally in rabbits are not remarkable; yet a cloudy swelling and moderately advanced fatty changes are often seen in the liver cells. There is also atrophy of the cells in severe cases with a protracted course, as well as edema of the reticulo-endothelial cells and generalized hyperemia. These facts account for the changes of liver margin that are frequently noted clinically. 5. The foregoing facts explain the onset of convulsions in severe forms of dysentery in the following manner: The bacterial toxin and abnormal products of decomposition that are formed in the intestinal tract and absorbed into the portal vein are first carried into the liver, causing a damage to hepatic functions of detoxication. Owing to this impairment of liver function, the ammonia which represents the intermediary product of protein metabolism is not changed into urea as in the normal liver; this causes a hyperammonemia which forms the direct exciting cause of convulsions. The author is not definite as to whether this hyperammonemia is the sole cause of the convulsion, for there are other substances to be considered such as dysentery toxin and other abnormal products of decomposition. In other words, while the author believes that there is a definite causative relation between the blood ammonia and convulsions in severe forms of infantile dysentery and experimental dysentery in rabbits, the exact position and course of this ammonia in bringing about convulsive attacks are yet to be determined. 6. Further experiments with endotoxins obtained from various types of dysentery bacilli, the adult rabbits show slight resistance as compared with young rabbits; this is also demonstrated by the oral administration of ammonia salts. This observation calls for more experimentation, but it at least indicates that the detoxicating function of the liver is greater in the young than in older rabbits.

KATO, Los Angeles.

DUODENAL PARASITES IN AN INFANT. K. SAKAI and M. CHIBA, J. Pediat. (Tokyo), Jan. 20, 1929, no. 344, p. 110.

The authors report an interesting case of duodenal parasites in an infant, aged 1⅓ years. Examination of the stools revealed the expulsion of a daily average of about 300,000 ova. Seventy-six parasites were expelled in the course of treatment with thymol and carbon tetrachloride. The anthelmintics were followed after each administration by either castor oil or an infusion of senna leaves. Of the seventy-six parasites, fifty-five were identified as *Ancylostoma duodenale* and only two as *Necator americanus*. The author expresses the opinion that the latter variety is the more amenable to treatment. The typical anemia showing 1,950,000 red cells and 10 per cent hemoglobin was improved until there were 3,130,000 red cells and 25 per cent hemoglobin.

KATO, Los Angeles.

Chronic Infections

THE FATE OF INTRAGLUTEAL INJECTIONS. LOREN W. SHAFFER, Arch. Dermat. & Syph. **19**:347 (March) 1929.

The gluteus maximus muscle consists of a bundle of numerous small muscles divided by septums of gluteal fascia and bound loosely into a whole by this fascia. Injections deposited within this muscle rupture to and follow the nearest fascial septum. Roentgenograms show that these injections have a curved linear distribution, being closely confined to the course of the fasciculi. Fluoroscopic study shows that oily suspensions spread rather slowly in from one to five minutes, depending on their viscosity, but that aqueous suspensions disperse to their final confines almost at once. Roentgenograms taken at intervals up to one week, after injections of iodized oil and bismuth salicylate, fail to show dispersion of the fluid after the first few minutes.

The upper outer quadrant is the area of election for injection, and the aim in depth should be the center of the gluteus maximus. If the injection is too superficial, leakage into the subcutaneous tissue is favored; and if too deep, the large veins running under the surface of the muscle are endangered. Injections passing entirely through the muscle should be avoided, as they may spread to produce irritation of the small sciatic nerve, and probably thus cause the common sciatic-like pain extending down the back of the thigh. Injections into the gluteus medius and minimus are not well tolerated because these muscles have fewer fascial septums and the injections are less well localized. Leakage backward along the needle tract with the subcutaneous formation of nodules can be prevented readily by using a small needle; by pulling the skin and subcutaneous fat to one side prior to injection; by making the injection well within the gluteus maximus; by leaving the needle in place for a few moments on completion of the injection, and by applying pressure with a cotton pledget immediately on its withdrawal.

SHIRLEY, Iowa City.

THE INCIDENCE OF TUBERCULOUS INFECTION IN SCHOOL CHILDREN. HENRY D. CHADWICK and DAVID ZACKS, New England J. Med. **200**:332 (Feb. 14) 1929.

The authors made a study based on an examination of 42,071 children who were given the Pirquet test. This piece of work was a part of a ten year program handled by the Department of Public Health of Massachusetts. The relations of infection to age, nationality, sex and history of contact were considered. At 5 years of age, 21 per cent were infected; at 10 years, 28 per cent; at 15 years, 35 per cent, and the average percentage for the whole group was 28 per cent.

Susceptibility to infection was equal in different nationalities. The two sexes were infected equally. The history of contact played an important part; approximately twice as many children react to the tuberculin test when there is a history of exposure. Persons with chronic tuberculosis infect more children than those with the acute form. The study shows that the number of infected children is becoming less.

GREEN, Denver.

OSTEOCHONDITIS LUETICA: COMPARISON WITH ANALOGOUS ZONES IN RICKETS AND INFANTILE SCURVY. RALPH S. BROMER, New England J. Med. **200**: 524 (March) 1929.

A splendid roentgenologic differentiation is presented, based entirely on the underlying pathologic processes. Changes in the long bones occur where the two normal processes of ossification take place, i. e., (1) where elongation of the diaphysis, endochondral ossification, occurs, and (2) where growth in thickness, endosteal or periosteal ossification, occurs. Rachitic changes reach their greatest manifestation in those portions of the skeleton which grow the fastest, i. e., in the costochondral junction, the distal ends of the femur and the ulna, and the proximal

end of the humerus. In infantile scurvy, the changes at the diaphyseal ends are apparent before the subperiosteal hemorrhages appear. In congenital syphilis, osteochondritis syphilitica appears practically always before periostitis syphilitica.

The three stages of osteochondritis syphilitica, as described by Wegner, are explained with reference to the work of other observers. In a similar manner the pathologic and roentgenologic changes in rickets and scurvy are described and compared with those in syphilis.

The author concludes that the roentgenographic appearance of endochondral bone growth, the diaphyseal ends, is definitely characteristic in the three diseases, and that the study of these areas is most important for the differential diagnosis.

GENGENBACH, Denver.

ARSENICAL REACTIONS IN CONGENITAL SYPHILIS COMPLICATED WITH ALKALOSIS. THURMAN B. GIVAN, New York State J. Med. **29**:132 (Feb. 1) 1929.

During seven years, thousands of injections of various drugs have been given to patients with congenital syphilis, with but two deaths due to the drugs used. In only five other patients have the reactions been sufficiently alarming to require hospital care. In three patients, two of whom died, the author noted a syndrome of vomiting accompanied by a coarse tremor of the hands and arms, and in one case by convulsions. Studies of the blood chemistry in the patient who recovered gave evidence of alkalosis. The author states his belief that this condition was present in the other cases.

AIKMAN, Rochester, N. Y.

AN UNUSUAL ERUPTION IN CONGENITAL SYPHILIS. C. RASCH, Brit. J. Dermat. **41**:155 (April) 1929.

Rasch comments on the occurrence of a special form of syphilitic eruption in children with congenital syphilis, and the diffuse infiltration of the skin, first observed by Trousseau and Lasègue in 1847. He presents reports of two cases that seem to form a variety of this disease not previously described. A boy, aged 1½ months, presented a pale reddish-brown eruption on all four limbs, on the nates and on the head and soles, that occurred as round, elongated and band-shaped, slightly infiltrated plaques which coalesced into irregular reticular lesions. This eruption was preceded by an extensive red dermatitis on the nates. The Wassermann reaction was positive. Fluid exuded by a punctured lesion on the leg revealed spirochetes. The eruption disappeared with antisyphilitic treatment although the Wassermann reaction remained positive. An infant, aged 2 months, who died two days after admittance to the hospital, presented the eruption on all the extremities. Red, desquamating plaques were noted on both palms; the soles were not affected. Tissue fluid revealed *Spirochaeta pallida*. Rasch feels that the condition is associated with the cutaneous veins, especially the second venous plexus, and may represent the first stage of the diffuse infiltration of the skin.

WIEN, Chicago.

DISCUSSION OF FIBROSIS OF THE LUNG IN CHILDREN. L. S. T. BURRELL, Proc. Roy. Soc. Med. **22**:271 (Jan.) 1929.

Tuberculosis of the lungs is rare in children except as part of general tuberculosis. During the first five years of life, general tuberculosis and surgical tuberculosis are common, but pulmonary tuberculosis is rare. From 5 to 16 years of age, all tuberculosis is rare. After the age of 16, tuberculosis of the lungs is common, and surgical tuberculosis is rare. Tuberculosis of the glands around the root of the lungs is frequently present in children, but the infection does not spread into the tissue of the lung. In these cases the disease is arrested, leaving behind some calcereous glands but no active disease. When the lung is affected, the spread is often rapid. The author gives the report of a girl, aged 13, who was taken suddenly ill with what was thought to be influenza. At the end of a fort-

night, harsh breath sounds were heard over the root of the left lung. The temperature was 98 F. in the mornings and 102 in the evenings. No tubercle bacilli were found in the sputum. A roentgenogram showed an opacity at the root of the left lung, and one taken three weeks later showed the spread of the disease. Bronchial breathing and bubbling râles were heard over the middle portion of the left lung. The sputum was loaded with tubercle bacilli. A left artificial pneumothorax was induced, and a year later the patient was free from symptoms.

This case illustrates the extreme rapidity with which tuberculosis of the lungs spreads in children. Absence of the tubercle bacilli from the sputum in the later stages is strong evidence against the disease being tuberculosis. Disease at the apex of the lung in children is usually nontuberculous. It is the catarrhal conditions that are important in children; they may follow measles, influenza and whooping cough. These conditions lead to destruction of tissue of the lungs and bronchi. As healing takes place by scar tissue, fibrosis results. Many children are known to be susceptible to colds or attacks of bronchitis. As time goes on, fibrosis takes place, and often bronchiectasis follows. Much can be done before the patient has developed any definite fibrosis. All sources of infection, such as the tonsils, teeth and gastro-intestinal tract, should be examined and treatment instituted when necessary. A vaccine is more successful in children than in adults. A long holiday will often effect a cure. Coddling is a mistake. Light clothing, sunlight, fresh air, good food and outdoor games should be recommended to keep the child in the best possible condition to prevent a recurrence of the condition.

WILLIAMSON, New Orleans.

THE PRINCIPAL TYPES OF INCIPIENT PULMONARY TUBERCULOSIS IN THE CHILD: ITS DIAGNOSIS THROUGH ROENTGENOGRAPHY AND INVESTIGATION OF THE BACILLUS. ARMAND DELILLE, Arch. españ. de pediat. **13**:5 (Jan.) 1929.

Initial forms of tuberculosis are now detectable with considerable accuracy, owing to improved diagnostic methods. Among these the most valuable roentgenoscopy and particularly roentgenography of the thorax, and study of the bacillus obtained from sputum, gastric lavage or homogenized sediment.

The author finds that pulmonary tuberculosis in the child is most frequently localized in the lobes of the lung. Of this localized form, he and his associates have demonstrated four principal types: (1) a caseous nodule with adjoining areas of consolidation, (2) lobar tuberculosis of the general bronchopneumonic type, (3) caseous lobar pneumonia and (4) the fusion of caseous areas with cavern formation.

Spontaneous healing of tuberculous pulmonary lesions is rarely observed in the child.

Demonstration of the tubercle bacillus in expectorated material is the only dependable proof of the presence of pulmonary tuberculosis. The author attaches much importance to the careful bacteriologic examination of material obtained by lavage. If the material is subjected to the process of homogenization, many more positive observations will be obtained.

SCHLUTZ, Minneapolis.

HEPATIC CIRRHOSIS WITH ASCITES AND SPLENOMEGALY: COMPLETE RELIEF FROM ASCITES UNDER ANTISYPHILITIC TREATMENT. JOSE BONABA and VICTOR RAGGIO, Arch. latino-am. de pediat. **18**:224 (March) 1929.

The condition developed at the age of 10 months. There was no history of syphilis in the family. The father was an alcoholic. The mother had two abortions previous to the birth of this child.

Considerable ascites and an enormous enlargement of the liver developed in the child. Both the tuberculin and the Wassermann tests gave negative results. Antisyphilitic therapy caused the complete disappearance of all abnormal symptoms. In spite of the absence of frank evidence of hereditary syphilis, the authors consider it as the probable etiologic factor in the case.

SCHLUTZ, Minneapolis.

THE FUNDAMENTAL IMPORTANCE OF EXTRAFAMILIAL INFECTION WITH TUBERCULOSIS IN CHILDHOOD. H. KLEINSCHMIDT, Gsndhtsfürs. f. d. Kindesalt. **4:** 103 (May) 1929.

Kleinschmidt wishes to define an intrafamilial infection as one which occurs in the household of the patient whether the infecting agent is or is not a member of the immediate family. He disagrees with Langer who reserves this term for superinfections, such as occur when one of the family residing in the household, is suffering from open tuberculosis. Kleinschmidt does not believe that the proximity necessary for these long continued infections is limited to members of the family. The same condition may be found outside the family, for example, when children visit in families in which open tuberculosis exists. Langer's definition, moreover, would tend to strengthen the layman's conception of tuberculosis as an inherited disease and would weaken the work of social service which attempts to limit the number of contacts between tuberculous patients and healthy members of the community.

REICHLE, Cleveland.

MANAGEMENT OF SYPHILITIC PREGNANT WOMEN: ITS RELATION TO THE PROGNOSIS FOR THE CHILD. WILHELM RICHTER, München. med. Wchnschr. **76:**735 (May 3) 1929.

The author makes a report on 187 pregnant women who had been under his care for four or more years. Of these, 104 gave positive serum reactions without a history of infection or clinical signs of the disease. They were treated with neoarsphenamine and bismuth. There were no miscarriages or premature births. New-born infants and blood from the umbilical vessels were examined as completely as present knowledge permits.

Richter found, in eighteen cases in which the mother received careful treatment up to the fifth month, that no stigmas occurred in the child. Without treatment after that time, the results were not so good, and when treatment was not given until the ninth month were of little value. The further back the beginning of the mother's syphilis the better the result. If the mother's infection was recent, but if she received careful treatment before the fifth month of pregnancy, the child was given injections of mercury and, later, of neoarsphenamine and bismuth. If the mother was infected four years or more before conception and received careful treatment before the fifth month, the child received no treatment.

SCHORER, Kansas City, Mo.

VACCINATION AGAINST TUBERCULOSIS; LANGER'S METHOD. J. W. MAKAROFF and W. M. FEDOROFF, Ztschr. f. Kinderh. **47:**396 (March 23) 1929.

After the vaccination of children by Langer's method (dose, 0.3 Gm. intradermally in three inoculations), a positive tuberculin reaction could be obtained in a high percentage of cases. The percentage depends, possibly, on the vaccine series (series A gave poor results), the dosage and the manner of using, but the questions relating to these demand further investigations. The children reacted positively to tuberculin for from two and one-half to twelve months, which marked the end of the observations. The clinical course of the tuberculin reaction was the same in the vaccinated children as in the children with tuberculosis, and the vaccination had no harmful results. In the vaccination of guinea-pigs, sensitiveness to tuberculin occurred with greater regularity than in the children and was correspondingly stable and lasting. The clinical course of the tuberculin reaction, the duration of allergy or the histologic structure of the tuberculin papule in the vaccinated guinea-pigs did not offer any firm basis for differentiation from the tuberculin reaction in animals with tuberculosis. In histologic structure, tuberculin papule occurred a midposition between the tuberculin papule and the coli papule of animals with tuberculosis. The differences, unfortunately, had a quantitative, not a qualitative, character. Vaccination did protect guinea-pigs from the severe generalized tuberculosis due to infection with Vallée's strain. The histologic

examination of the organs permitted, as far as the small amount of material allowed one to judge, the recognition of the fact that the productive character of the tuberculous process in the vaccinated guinea-pigs was more outspoken than in the control animals.

EMERSON, Boston.

THE COSTA REACTION IN TUBERCULOSIS IN CHILDHOOD. K. NÜSSEL and H. HELBACH, Ztschr. f. Tuberk. **52**:301, 1928.

The reaction is less sensitive than the sedimentation reaction of erythrocytes, but it is recommended particularly for examination of children because it requires only a small amount of blood.

MAX PINNER.

PSYCHIC CHANGES IN TUBERCULOUS CHILDREN. T. P. SIMPSON, Collected Papers, Psychiatric Clinic of the First Moscow State University **2**:71, 1927.

The extensive literature dealing with the personality changes in tuberculous children is reviewed by the author. Two groups of children were studied. The first group consisted of 158 children with bovine tuberculosis and also with a scrofulous diathesis who were living at home and were attending a fresh air school. The second group consisted of forty children with pulmonary tuberculosis in a sanatorium. The children were studied in great detail by physicians, psychologists, sociologists and school teachers. Anthropologic studies were done according to Kretschmer's classification. Medical studies included the use of fluoroscopy, x-rays, various biologic reactions and blood tests. The psychologic studies consisted of measurements of intelligence, association tests, analysis of dreams and an analysis of behavior charts in school and at home. Heredity was studied back for four generations, and the ancestors were classified in accordance with Kretschmer's conception of personality types. Seventy-six per cent of the families were essentially cyclothymic; 16 per cent, schizoid and 8 per cent mixed. In 47 per cent of the cases there was a history of mental disease in one or more ancestors. Anthropologic studies showed an asthenic type in 40 per cent of the cases. Dermographia, increased tendon reflexes and absence of conjunctival and corneal reflexes were observed in more than 50 per cent of the cases. There was usually fair intellectual development but marked reduction in attention and memory. The children were characterized by egocentrism, facility of speech and ease of verbal expression with rather shallow brilliancy. The imaginative faculty was well developed. The artistic production of the children, as well as their dreams, showed a marked feeling of isolation from the rest of the world. In the affective sphere, the children were extremely sensitive and rather sentimental. There was a good deal of irritability with quick responses to various stimuli, but the responses lasted a very short time and became quickly exhausted. The reaction of fear was extremely common. As far as psychomotor reactions are concerned, the author found two sharply differentiated groups of the hyperkinetic and the hypokinetic types. The mechanisms described by Adler in connection with the feeling of physical inferiority were very common. A study of the personality of the children showed that 43 per cent had a schizoid personality, 20 per cent a cyclothymic and 11 per cent a psychopathic personality. There is a high degree of correlation between the severity of the disease and the personality type of the child. In the severe forms of intoxication the schizoid type of personality is most common. All these data refer to the children of the first group.

The children with pulmonary infections were studied with less detail on account of their condition. In most of the children, the author observed a marked psychomotor retardation. In this group there was commonly found a clinical picture suggestive of definite involvement of the central nervous system, so that some of the children looked as if they had a tumor of the brain or paresis.

The author feels that a tuberculous infection changes the personality of a child in the sense of "schizoidization" of the sick child.

KASANIN, Boston.

Internal Diseases

CHRONIC BRONCHIECTASIS IN CHILDHOOD, WITH OBSERVATIONS ON EARLY DIAGNOSIS. EDWARD S. THORPE, JR., Am. J. M. Sc. **177**:759 (June) 1929.

The author reviews a series of fifty-three cases of bronchiectasis in children less than 13 years of age, occurring in a period of five years. He considers this condition far more common than is usually supposed. He states that bronchopneumonia, pertussis and measles are the common factors in the production of bronchiectasis, as they carry the infection deep into the framework of the bronchi and the lungs. Disease of the accessory sinuses is thought to be a concomitant factor in maintaining a state of sepsis. He attempts to demonstrate the protean nature of the disease and to correlate the physical data with the pathologic lesions, especially in early cases.

Evidence is presented to show the damaging effect of the disease on the nutritional state of the children. Chart 1 gives an analysis of the symptoms, the physical signs, and the roentgenologic and bronchoscopic observations for the thirty children who were examined with a bronchoscope; chart 2 an analysis of the observations on twenty-three patients not examined with a bronchoscope.

The author expresses the opinion that if all patients suspected of having suppurative bronchitis were treated bronchoscopically and were not given cough mixtures, bronchiectasis would be a rarity. He demonstrates that the principal points in the treatment are postural drainage, breathing exercises, plenty of nourishing food, cod liver oil, fresh air and adequate heliotherapy. An early diagnosis is used to make the therapeutic program more efficient.

HENKE, Omaha.

ROENTGEN DIAGNOSIS OF LESIONS OF THE UPPER URINARY TRACT UNASSOCIATED WITH CALCULUS. W. M. SHAW, Am. J. Roentgenol. **17**:426 (April) 1927.

An ordinary flat film reveals little more than calculus. The pyelogram properly made and interpreted offers the most valuable and conclusive proof of a larger number of renal lesions than any other diagnostic effort. It is of diagnostic value in the normal kidney, in hydronephrosis, pyelitis, pyonephrosis, renal tuberculosis, renal and ureteral anomalies, cystic kidney, the identification and localization of renal shadows, the identification and localization of ureteral obstruction, and renal tumor.

STULIK, Chicago.

A ROENTGENOLOGIC SIGN OF MUCOUS COLITIS. A. W. CRANE, Am. J. Roentgenol. **17**:416 (April) 1927.

The author describes and shows roentgenograms of a "barium string" which may be found in any portion of the colon, most frequently in the descending colon, but rarely in the sigmoid and ascending colon. It cannot be explained as traces of barium adhering to the colonic mucosa. This sign may be pathognomonic of mucous colitis, but occurs with spasticity of the colon, psychoneuroses and abdominal pain. The author concludes that the barium string is a more frequent and definite sign of this nonsurgical cause of abdominal pain. If these signs of mucous colitis can be verified by other roentgenologists, there will be established the curious fact that the colon contains roentgenologic evidence of a psychoneurosis.

STULIK, Chicago.

DIABETIC EXOPHTHALMIC DYSOSTOSIS. L. HAUSMAN and W. BROMBERG, Arch. Neurol. & Psychiat. **21**:1402 (June) 1929.

In a report of one case, with a review of fifteen collected from the literature, the authors state that the question remains whether the syndrome of diabetes insipidus, exophthalmos and disease of the membranous bones is the result of some degenera-

tive, toxic, inflammatory or metabolic process in which infection or trauma is the exciting factor. Particular significance attaches to the dysostosis in relation to the mechanism of diabetes insipidus. From the evidence at hand, it seems that this ossous selectivity is linked up with some metabolic, endocrinal or neurogenic regulatory mechanism in an anterior portion of the hypencephalon.

SANFORD, Chicago.

THE CHILD WITH POTENTIAL HEART DISEASE. C. G. KERLEY, J. A. M. A. **92:** 517 (Feb. 16) 1929.

A certain type of child is particularly susceptible to the infecting agencies causing heart disease. Three groups of these children may be recognized: those who have had or who have rheumatic fever; those who have had or have chorea, and those who complain repeatedly of pain in the extremities, unaccountable on a basis of trauma or of disease. Heart disease in children so affected may be prevented in many by the eradication of disease foci, first with a persistent and later with an interrupted use of salicylic acid, alone or combined with alkali.

BONAR, Salt Lake City.

URETERAL OBSTRUCTION IN INFANCY. MEREDITH F. CAMPBELL and JOHN D. LYTTLE, J. A. M. A. **92:**544 (Feb. 16) 1929.

About 2 per cent of infants are found to have ureteral obstruction that predisposes to infection and renal obstruction. When pyuria resists systematic therapy for more than four weeks, a complete urologic investigation is indicated. With this criterion the authors have disclosed gross disease of the urinary tract in more than 95 per cent of the patients examined. The same urologic procedures used in adults should be employed in children and infants if the small caliber of the instruments permits.

BONAR, Salt Lake City.

ACUTE LARYNGOTRACHEOBRONCHITIS. HARRY L. BAUM, J. A. M. A. **91:**1097 (Oct. 13) 1928.

From the study of twenty-four cases of acute laryngotracheobronchitis of such severity as to necessitate intubation, the author came to the following conclusions: This serious condition should be more clearly recognized by physicians; early diagnosis will result in hospitalization, and intervention may prevent more serious developments; the grave importance of the exhaustion factor in partial laryngeal obstruction should be emphasized; the prognosis should be guarded because of the possibility of a fatal terminal bronchopneumonia; intubation is the operation of choice as the primary procedure in these cases, and bronchoscopy should be resorted to as soon as signs of bronchial obstruction appear.

BONAR, Salt Lake City.

CRUPOUS PNEUMONIA AND BRONCHOPNEUMONIA. J. P. CROZER GRIFFITH, J. A. M. A. **91:**1331 (Nov. 3) 1928.

A study of twenty-six cases was made, in which a diagnosis of pneumonia had been made during life by either clinical or roentgen examination, or by both, all the cases having come later to autopsy. The clinical, roentgen and postmortem diagnoses agreed in only six of the twenty-six cases. In ten cases the clinical and roentgen diagnoses agreed, but in four of these neither diagnosis was correct. In sixteen cases the clinical and the roentgen diagnosis disagreed; among these the clinical diagnosis was correct in nine instances, the roentgen diagnosis in six, and neither of them in one. It was concluded that both the physical and the roentgen observations are of value, but that neither can be accepted beyond doubt in many instances. When the two agree, the probability of correct diagnosis is greatly increased.

BONAR, Salt Lake City.

THE PRESENT STATUS OF PYELITIS IN CHILDREN. LOUIS BARASH, Internat. Clin. **2**:159 (June) 1929.

The author presents a brief historical review of the literature on pyelitis, recognized and described as a clinical entity by Rayer, in 1837. Pyuria is usually secondary to an infection. Various theories of implantation and propagation of the infecting organism are disclosed. Several authorities are quoted to show that the essential factors are a focus of infection and obstruction to the urinary outflow. Especially emphasized are: the rôle of anatomic abnormalities, such as stricture of the ureter, the valvelike action of the intravesicular portion of the ureter and the phenomenon of "reflux."

In congenital cases, there is a predominance of infection in boys. The anatomic lesion of pyelitis is difficult to determine because experimental cases are associated with some other condition, such as cortical and medullary abscesses. The well recognized symptoms of pallor, restlessness, remittent fever, and others are enumerated.

Pyelitis is occasionally a self-limited disease or is cured spontaneously with the subsiding of an acute parenteral infection. Alkaline therapy is considered empiric and its rationale vague. Hexamethylenamin, from 0.5 to 1 Gm. every four hours, is usually well tolerated but may produce irritation. General care of the child such as protection against nasal and aural infections, is important. In intractable cases, in which rational treatment is given, cystography and pyelography may show organic changes, such as hydronephritis, hydro-ureter, ureteral stricture or calculi.

A complete history should be obtained and repeated examinations of the urine, tests for kidney function and blood chemistry tests should be made before the cystoscope is used.

MILLER, South Bend, Ind.

PAROXYSMAL HEMOGLOBINURIA: A REVIEW. G. M. MACKENZIE, Medicine **8**: 159, 1929.

For many years there was no differentian between paroxysmal hemoglobinuria and a number of others, such as intermittent hematuria and conditions manifesting hematuria, notably malaria. Harley (1865) reported a case in which the patient was "cured by mercury and quinine," without knowing the rôle of syphilis, or the nature of the coloring matter. Rosenbach (1880) showed that an attack could be produced by immersion of the patient's feet in ice water for ten minutes. Subsequently, a fairly large number of cases were reported, each author emphasizing some more or less important phase or symptom. In 1904, Donath and Landsteiner made a thorough study of the disease both clinically and in the laboratory; relatively little of significance has been added to their studies, except the important observation, possible only after the discovery of the Wassermann reaction in 1906. that all genuine examples of paroxysmal hemoglobinuria are of syphilitic origin.

The symptomatology involves the manifestation of an attack, the chronic effects of loss of blood, and any late manifestation of syphilis, congenital or acquired. By means of the Wassermann reaction, syphilitic infections can be demonstrated in more than 90 per cent of the cases. In most instances, clinical evidence of syphilis may be found. "The large percentage of congenital syphilitics among the reported cases indicates that the congenitally infected individual is more liable to develop hemoglobinuria than those with the acquired diseases . . ." "Several authors have reported more than one case in the same family. The disease appears to be relatively common in Japan." The patient first reports the passage of dark, almost black, urine and calls it "bloody urine." He usually states that it followed exposure to cold. The interval between the chilling, however, slight, and the paroxysm varies from a few minutes to eight hours. There are also apt to be aching pains in both legs or in the abdomen, abdominal cramps, headache and malaise. A chill and a rise in temperature of from 102 to 104 F. occur, but cases are recorded in which these observations are lacking. The temperature may be elevated briefly, or for many hours, and the first urine passed following the chill is highly colored. The color varies in depth according to the

amount of oxyhemoglobin, methemoglobin and hematin present. The urine may be dark for only one or two passages or for several days. "Rose-colored urine" has been observed following spontaneous paroxysms or a cold foot bath.

In these cases the urine contained uro-erythrin. Following the severe attacks, slight icterus may be noted. Enlargement of the spleen is not unusual after severe attacks. Occasionally, a transient enlargement of the liver is observed.

The degree and duration of chilling necessary to produce an attack are highly variable. Exertion sometimes precipitates attacks; such cases are of doubtful syphilitic origin. Emotional states have been said to produce attacks, but the evidence has not been conclusive.

Although the color is due to oxyhemoglobin, methemoglobin and hematin, specimens examined immediately after a paroxysm may show a few intact red cells. "Ghosts" of erythrocytes may be so abundant as to settle to a heavy sediment. Albumin is present. Red blood cell casts have been noted. Eason found the urea nitrogen in the urine to be 99.6 per cent of the total nitrogen during a paroxysm, and the following day 86.4 per cent; the day before the attack it had been 83.5 per cent of the total nitrogen. Abortive, rudimentary, frustrated or larval attacks are terms to designate many variations from the typical cause of paroxysms.

Hives may precede an attack. Raynaud's syndrome is one of the commonest occurrences. The fingers, toes, tips of the nose, lips or ears may be blanched or cyanotic. Urticarial wheals are common. Vesicles may appear following chilling. Changes in systolic and diastolic blood pressure may precede the paroxysm.

Theories of the serologic mechanism are: (1) absorption of the lysin by the erythrocytes in the cold, and (2) lysis of the sensitized erythrocytes at a higher temperature if the complement is present (?). The discussion of this phase is lengthy and technical and not adaptable to a review. The author gives the pathogenesis in relation to syphilis as follows: 1. Paroxysmal hemoglobinuria is usually, and perhaps always, a manifestation of syphilis. 2. A small percentage of patients with late syphilis have the latent form of paroxysmal hemoglobinuria. There is definite hemolysin.

The liberated hemoglobin is converted into bilirubin. One may conclude from the experiment of Jones that under the conditions of the observations urobilin is formed in the liver from bilirubin which is formed from hemoglobin. Jones and Jones also demonstrated, in a patient with paroxysmal hemoglobinuria, the extrahepatic formation of bilirubin; they showed that it was present in the blood peripheral to a ligature after the ligatured arm had been immersed in cold water.

Nearly all patients with paroxysmal hemoglobinuria have either a moderate or a severe anemia during the period of the year when attacks occur, the severity depending on the progress and severity of the attacks. The erythrocytes are decreased as is the hemoglobin during an attack, both to a varying extent. Various changes indicative of anemia occur in the red blood cells after a paroxysm. Marked and interesting changes occur in the leukocyte count during an attack. In cases studied by the author a leukopenia occurred within fifteen minutes after a paroxysm. There was a relatively transient lymphocytosis followed by a leukocytosis with a higher percentage of neutrophils than was present before the paroxysm. The theory of Uchida, that the blood changes are due to derivatives of hemolyzed erythrocytes, appears to be well founded.

Whereas cases have been reported in which no improvement followed antisyphilitic treatment, it is probable that the patients were not treated thoroughly. Antisyphilitic treatment offers the best results.

ROYSTER, University, Va.

OCCURRENCE OF SUBACUTE BACTERIAL ENDOCARDITIS IN CHILDHOOD. GEORGE M. LAWSON and ROBERT S. PALMER, New England J. Med. **199**:1205 (Dec. 13) 1928.

Reports and discussions are given for four cases, with postmortem observations in two; all of the patients died. The literature on the subject is reviewed. The authors explain their method of bacteriologic differentiation of blood cultures in

which *Streptococcus viridans* is found, based on the manner of its growth, into two groups: the first a heterogeneous group of diseases — arthritis, rheumatic fever, terminal septicemia, sinus infections and similar conditions — and a second group, cases of subacute bacterial endocarditis. The youngest patient whose case was recorded in the literature was 5 years of age.

GENGENBACH, Denver.

SOME SIDE LIGHTS ON THE THYMUS VOGUE. JOSEPH GARLAND, New England J. Med. **200**:59 (Jan. 10) 1929.

The author apparently does not believe in the importance of the enlarged thymus gland as a source of danger. Simple enlargement may cause symptoms, presumably like those of a tumor mass in the mediastinum. Status thymica lymphaticus, a rare condition (some authors doubt its existence as an entity), may be confused with simple hyperplasia of the thymus. "There are no acceptable standards of normality or abnormality of the thymus gland by x-ray, because even at autopsy the gland by weight is subject to variations which permit only of average figures being made as partial guides to go by." The author also suggests that the enlarged thymus or persistently enlarged thymus, as evidenced by roentgen examination, may not even be a definite abnormality. A lymphadenitis of the upper mediastinum may resemble an enlarged thymus in the roentgenogram, and may be the cause of certain symptoms attributed to enlargement of the thymus. Certain modern studies seem to point to the suprarenal glands as participating in sudden death, discrediting the theories concerning the thymus or status lymphaticus.

Autopsy records at the Massachusetts General Hospital have convinced the author that the present vogue of roentgen examination of the thymus and of irradiation of all patients in whom a shadow appears would seem to be unjustified.

GREEN, Denver.

SPONTANEOUS PNEUMOTHORAX IN CHILDREN UNDER TWO YEARS. B. BASHINSKI, South. M. J. **22**:525, 1929.

The author reports two cases of pneumothorax which developed in connection with lobar pneumonia. There was serous or purulent effusion in both. Neither case was due to perforation of the lung by an aspirating needle, a fracture rib or a tuberculous focus.

There are three kinds of pneumothorax: the open, closed and valvular types. If the pneumothorax is open, there is little enlargement of the affected side. The heart is always displaced. The percussion note is tympanitic when the pneumothorax is closed. There usually are no râles.

SCHLUTZ, Minneapolis.

EXUDATIVE DIATHESIS AND HEMOTHERAPY. PAUL FERNANDEZ CORDOBA, Arch. am. de med. **5**:43 (April) 1929.

The author recommends the use of injections of whole blood intramuscularly in exudative diathesis, according to the method of Leon Velasco Blanco. From 3 to 5 cc. is injected at intervals of from one to two days. The blood is usually taken from the mother. Although few cases are reported, the author is impressed with the effectiveness of the injections.

SCHLUTZ, Minneapolis.

HEMORRHAGIC PLEURISY IN THE CHILD. LUIS MORQUIO, Arch. españ. de pediat. **13**:65 (Feb.) 1929.

The condition is rare in children. The author reports six cases in which it was either a complication or a primary condition. It occurred in connection with such conditions as post-typhoidal purpura hemorrhagica, acute pleuropulmonary tuberculosis, and acute postoperative abdominal disorders.

In one case, a malignant neoplasm of the thymus gland with pleural metastasis caused the disorder. In another, it was due to trauma, although there was no

discernible injury to either the pleura or the ribs. Diagnosis of the condition is not easy, and is definitely established only by thoracentesis.

The author has observed that the prognosis in the tuberculous form is not always unfavorable. The outcome in the nontuberculous and nonmalignant form is generally favorable.

SCHLUTZ, Minneapolis.

RHEUMATIC CARDITIS WITH COMPLETE HEART BLOCK. FAMILIAL AMYOTONIA CONGENITA. WILFRED SHELDON, Proc. Roy. Soc. Med. **22**:638 (March) 1929.

A case of rheumatic carditis was reported in a girl, aged 5 years, who had been in good health until October, 1928, when she complained of vague pains in her limbs. In November, she was found to have a systolic and a mid-diastolic murmur at the apex, and the heart was moderately enlarged. An electrocardiogram showed a complete auriculoventricular block. The auricles were beating at the rate of 84 per minute and the ventricles at 44 per minute. No evidence was found to favor a diagnosis of congenital morbus cordis.

Familial amytonia congenita was reported in a boy, aged 3½ years, who was the fifth child in the family. Two of his brothers, the first and second in the family, suffered from the same disease; the third and fourth children were in good health.

WILLIAMSON, New Orleans.

TWO CASES OF ANEMIA SHOWING THE RESULT OF LIVER TREATMENT. BERNARD SCHLESSINGER, Proc. Roy. Soc. Med. **22**:649 (March) 1929.

An infant, aged 7 months, showed a red blood cell count of 1,752,000 and 20 per cent hemoglobin on June 29, 1928. Liver extract, 0.5 drachm (1.8 cc.), was given twice a day. On August 22, the red blood cells numbered 5,264,000 and the hemoglobin content was 50 per cent. The other case of anemia occurred in a girl, aged 6 years. On Oct. 9, 1928, her blood showed 4,664,000 red blood cells and 30 per cent hemoglobin. She was given a diet of liver. On December 18, the red blood cells had increased to 5,288,000, and the hemoglobin content was 40 per cent. The author felt that liver therapy would produce a definite improvement in the condition of the blood in rickets and that it should always be tried when anemia is found in association with rickets.

WILLIAMSON, New Orleans.

RHEUMATOID PURPURA COMPLICATED BY INTUSSUSCEPTION AND VOLVULUS. J. F. CAIZERGUES, Nourrisson **17**:99 (March) 1929.

This combination of serious diseases occurred in a girl, aged 3 years. At the outset there was gastro-intestinal disturbance, with painful joints, a little fever and a purpuric eruption on the legs. On the fifth day the abdominal symptoms became acute, and a sausage-shaped mass in the abdomen could be palpated. No bloody mucus appeared in the stools. At operation a volvulus and an intussusception, both involving the ileum, were found and relieved. The patient recovered, but at the time of the report still had a fecal fistula. The author expresses his belief that the volvulus prevented the passage of bloody mucus from the invaginated intestine.

MCCLELLAND, Cleveland.

BORDERLINE CASES OF PERNICIOUS AND APLASTIC ANEMIAS AND LEUKEMIAS. D. OPITZ, Arch. f. Kinderh. **86**:293 (March 28) 1929.

Opitz points out the difficulty of diagnosing leukemias and the primary anemias in the early stages. In the aleukemic intervals of leukemia, the general condition of the patient is not much disturbed; the temperature may be subfebrile; lymphocytosis does not yet dominate the blood picture; myeloid cells are not numerous, and thrombopenia, hemorrhages and necrotic changes in the oral cavity may be

absent. The case report at times does not suggest leukemia. The condition may begin acutely like an infectious disease, subacutely with pains in various bones and joints, or insidiously with increasing paleness, weakness and loss of appetite.

SANFORD, Chicago.

TREATMENT FOR TAPEWORM IN CHILDREN. P. KARGER, Med. Klin. **25**:745 (May 10) 1929.

Successful treatment for tapeworm in children is rather difficult. The best drug is aspidium. The dosage is from about 6 to 8 Gm., irrespective of age. It has to be followed by a cathartic. A difficulty always encountered is that children will vomit the drug, owing to the disagreeable taste.

Schneider, in 1926, recommended the use of the duodenal tube for giving aspidium. This can be easily done with the usual technic. The duodenal tube is introduced into the stomach through the nose, the upper end being fixed with adhesive tape to the cheek. It is left in the stomach for about four hours. After this time, the end of the tube is in the duodenum and the drug can be given. With this method, failures are extremely rare; the children do not vomit, and the worm is usually expelled with the head.

ZENTAY, St. Louis.

EPIGASTRALGIC SYNDROME OF VERTEBRAL AND INTRAVERTEBRAL ORIGIN. WITTING, Arch. d. mal. de l'app. digestif. **19**:133 (Feb.) 1929.

Among the many causes of epigastric pain simulating gastro-intestinal disorders, Pott's disease and intravertebral tumors must be considered. The author gives the history of one case in which Pott's disease simulated the picture of a gastric ulcer. In another patient who had abdominal pains, a diagnosis of appendicitis and duodenal ulcer was made and an operation performed. The condition was recognized finally as an intravertebral tumor which was later removed.

The diagnosis has to be made in two phases: 1. It has to be shown that the picture does not correspond to any known digestive disorder. The general characteristics are as follows: The pain persists and is not influenced by any digestive therapy. The anatomic and functional examination of the stomach and of the duodenum gives negative results. Usually there are diffuse abdominal pains present that cannot be attributed to the upper digestive tract. 2. One has to look for possible neurologic signs of the processes mentioned as the cause of the trouble.

The mechanism of the disorder may be explained by either continuous or intermittent irritation of vertebral segments which directly or reflexly produce spasmodic contractions of the stomach, hypersecretions and pain, or by irritation of sensory fibers through the digestive functions of the affected organs. This irritation may be intermittent, owing to repeated hyperemia at the time of digestion.

ZENTAY, St. Louis.

PNEUMOCOCCIC PERITONITIS: REPORT OF A CASE. A. LACKA and C. ROZENGARTENOWNA, Pediatria Polska **9**:43 (Jan. and Feb.) 1929.

Pneumococcic peritonitis occurred in a boy, less than 1 year of age, and lasted for six weeks. According to the author's statistics, this condition seldom occurs in boys at that age. The diagnosis is difficult. The cause in the present case was unknown, because at postmortem examination the appendix was found to be normal.

KRUPINSKI, Chicago.

BILATERAL PYONEPHROSIS WITH CALCULI IN AN INFANT AGED THIRTEEN MONTHS. A. LACKA and C. ROZENGARTENOWNA, Pediatria Polska **9**:46 (Jan. and Feb.) 1929.

Bilateral pyonephrosis with calculi is a rare condition and, according to Hutinel, occurs in children artificially fed, mostly on milk, and in children with diarrhea.

KRUPINSKI, Chicago.

Nervous Diseases

BEHAVIOR DIFFICULTIES IN CHILDREN ASSOCIATED WITH THE RESULTS OF BIRTH TRAUMA. PAUL L. SCHROEDER, J. A. M. A. **92**:100 (Jan. 12) 1929.

Behavior problems, the direct result of mental retardation, are greatly influenced by difficult labor. Distractibility and hyperactivity are characteristic personality traits in birth trauma, but no behavior difficulty is specific. Children with cerebral birth injuries but no palsies show behavior characteristics and mental retardation similar to those with birth palsies. Variation in behavior characteristics is dependent on the orthopedic handicap. Children with cerebral injury at birth who show distractibility and hyperactivity but no palsies should be included in the classification of the results of birth trauma.

BONAR, Salt Lake City.

CISTERN PUNCTURE. LEO JACOBI, Arch. Dermat. & Syph. **19**:650 (April) 1929.

The author advocates an indirect method of cisternal puncture rather than the direct method standardized by Ayer and his associates and now in common use. By the direct method, the needle is introduced without touching bone. By the indirect method the posterior border of the foramen magnum is located first with the needle and is used as a point of orientation. It is felt that the preliminary orientation decreases the dangers of cisternal puncture. The method is described in detail.

SHIRLEY, Iowa City.

ENCEPHALITIS PERIAXALIS DIFFUSA. W. D. SHELDEN, J. R. DOYLE and J. W. KERNOHAN, Arch. Neurol. & Psychiat. **21**:1270 (June) 1929.

The authors present two cases, one in a boy, aged 7, and the other in a woman, aged 27. The first case was a classic example of Schilder's disease. The evolution of symptoms and signs, commencing with a change in personality and a diminution in auditory and visual acuity, followed by convulsions, evidence of involvement of the pyramidal tracts and, finally, quadriplegia with dementia, was indicative of widespread cerebral injury. The steadily progressive course in the second case with unilateral signs and increasing intracranial tension resembled, in a general way, a later case reported by Schilder.

SANFORD, Chicago.

INCREASED INTRACRANIAL PRESSURE. JOHN S. B. STOPFORD, Brain **51**:427 (Dec.) 1928.

Stopford shows that there is rarely any primary obstruction of the aqueduct in cases of supratentorial tumor. If present, the obstruction is probably due to direct pressure on the aqueduct by growth as in some cases of pinealoma or occlusion by the neoplasm itself. He believes that the raised intracranial pressure associated with tumors above the tentorium was originally caused by deflection of the falx and consequent compression of the great vein of Galen, which induces an excessive production of cerebrospinal fluid. Tumors below the tentorium may more readily obstruct the outflow of cerebrospinal fluid from the ventricular system, but in cases in which no block is present the author states that the cause of the raised intracranial pressure may be due to elevation of the tentorium, with consequent compression of the great vein of Galen. Raised intracranial pressure associated with tumors within the cranium is more commonly due to compression of the great vein of Galen than to any other cause. "Whilst obstruction to the venous drainage from the choroid plexuses or block in the region of the aqueduct or fourth ventricle, separately or in association, probably explain the origin of the raised intracranial tension," other factors of secondary importance merely increase the already raised pressure. A bibliography completes the article.

LUCAS, San Francisco.

SOME DISORDERS OF NEURO-MUSCULAR COORDINATION IN CHILDREN. F. S. LANGMEAD, Brit. J. Child. Dis. **26**:1 (Jan.-March) 1929.

The author groups together disorders affecting "tubes the musculature of which is unstriated. Above a certain zone in their continuity are to be found all the

evidences of obstruction at that level . . . yet no cause of obstruction is manifest." In this group of idiopathic dilatations and hypertrophies he includes: (1) those of the esophagus ("achalasia of the cardia" or "cardiospasm"); (2) those of the colon ("Hirschsprung's disease"); (3) those of the bladder and ureters, and (4) idiopathic hydronephrosis.

The cause is ascribed to a disorder of the nervous control, congenital in some cases.

The author is accustomed to think of pyloric spasm and hypertrophic stenosis in infants as different degrees of the same defect. He states that the existence of the hypertrophied sphincter affords sufficient reason for separating hypertrophic stenosis from the idiopathic dilatations, but then again he finds that pyloric spasm without hypertrophy is obviously similar to the disorders which he includes in his classification.

In idiopathic esophagectasis and also in idiopathic dilatation of the colon, several investigators recently found destructive changes inflammatory in character in Auerbach's plexus. The speculation still exists as to whether this will explain these conditions.

LANGMANN, New York.

ACUTE MENINGO-ENCEPHALOMYELITIS OF CHILDHOOD. W. RUSSELL BRAIN and DONALD HUNTER, Lancet **1:** (Feb. 2) 1929.

The authors made their observations on six patients ranging in age from 3 to 18 years, all developing their symptoms within a period of six weeks and all except one living in East London. All showed an acute onset and all but one made a practically complete recovery; in the patient with the mildest case recovery occured within four days and in the one most severely affected, in whom meningeal signs were insignificant compared to the extensive involvement of the cerebral hemispheres leading to complete aphasia and double hemiplegia, several months were required for recovery.

The condition differed from encephalitis lethargica in that the onset was fulminating; in that cervical rigidity, Kernig's sign and trismus were present, and in that there was an absence of ocular abnormalities. On the other hand, it resembled in many respects the numerous reported cases of postvaccinal encephalitis. Both show a tendency toward complete recovery of the patients who survive.

Postmortem examination of the boy, aged 3 years, who died of the disease, showed ring hemorrhages in a congested and edematous brain, lipoid nephrosis of the kidneys and extreme fatty, partly lipoid degeneration of the liver.

The author considers that the cases studied fall into the third group of the following classification:

1. Cases characterized by acute degeneration of the ganglion cells of the brain with hyperemia and often marked edema but without macroscopic hemorrhages.
2. Cases in which multiple macroscopic hemorrhages are the conspicuous feature.
3. Cases characterized by vascular demyelination.

LANGMANN, New York.

A CASE OF POSTDIPHTHERITIC POLYNEURITIS. M. DA ROCHA, JR., Arch. de pediat., Rio De Janeiro **2:**202 (March) 1929.

A child, aged 7 years, had a moderate case of diphtheria, which was relieved by a small dose of antitoxin. Three weeks later paralysis of the soft palate occurred, followed by some paralysis of the extremities. The condition responded well to small doses of strychnine. Da Rocha believes that this treatment is specific, but that the prophylaxis is of great importance. This consists of treating patients with diphtheria with sufficient antitoxin to cover thoroughly any possible emergency. A minimal dose, therefore, would be 100,000 units.

SANFORD, Chicago.

MIGRAINE IN EARLY INFANCY. O. DE OLIVEIRA, Arch. de pediat. (Rio de Janeiro) **7**:237 (April) 1929.

From a review of the literature and from his own experience, Oliveira concludes that migraine is rare in early infancy. There is usually a history of some hereditary nervous disorder in the family. The symptoms are similar to those in migraine of the adult, and the treatment is essentially the same. A brand of amidopyrine, U. S. P., and phenobarbital are probably the best sedatives. The prognosis is not good, as the condition usually indicates a potential morbid disorder.

SANFORD, Chicago.

CHOREA MINOR. WERNER GOTTSTEIN, Klin. Wchnschr. **6**:2121, 1927.

The author presents an interesting review of the history, the problem of diagnosis and the methods of treatment of chorea minor. The quieting treatment of the present day is in marked contrast to the vigorous methods of the Middle Ages.

In addition to the continuous involuntary movements and the lack of coordination seen in chorea, the disturbance of reflex actions is to be noted. For instance, the abdominal muscles are frequently pulled in during inspiration, thus acting in direct opposition to the attempts to enlarge the thoracic cage by descent of the diaphragm. Choreic symptoms may occur with injury or tumor of the brain. Their occurrence in encephalitis has suggested to some writers that chorea should be considered as a subdivision of that disease. The author states his belief that little is known of the pathologic histology; he does not mention Homer Swift's work in that field.

In medication, von Roder's treatment with phenylethylhydantoin is considered. It is given in daily doses of 0.3 Gm., until the development of an exanthem. In this connection, it has been noted from time to time that chorea disappears with the development of an acute exanthematous disease. Studies made by von Roder of the blood of patients with exanthematous diseases and of those to whom phenylethylhydantoin was given showed an increasing alkalinity before the appearance of the rash, which gave place to an acidity at the time of the eruption.

In addition to caring for the patient with chorea where he may be quiet and undisturbed, the author sanctions the use of bromides, phenobarbital and arsenic. He emphasizes the fact that the individuality of the patient must be considered in all cases.

LESLIE, Evanston, Ill.

THE STEP-PARENT. C. HOENIG, Ztschr. f. Kinderforsch. **35**:187 (April 23) 1929.

In an article of 142 pages, the author gives a detailed description of 41 cases in which conflicts had arisen between children and their step-parents. The conclusions contain nothing new.

REICHLE, Cleveland.

METHODS FOR MASS EXAMINATION OF THE MOTOR FUNCTIONS OF CHILDREN AND MINORS. N. I. OSERETZKY, Ztschr. f. Kinderforsch. **35**:332 (April 23) 1929.

Methods are described by which the author hopes to standardize the tests for motor functions: static and dynamic coordination, speed, synchronic movements, strength and synkinesis. It seems doubtful whether Oseretzky's technic, with its complexity and tediousness, is applicable to children.

REICHLE, Cleveland.

INNER SPEECH. A. KERN, Ztschr. f. Kinderforsch. **35**:420 (April 23) 1929.

Inner speech is a phenomenon which every one can observe in himself. It consists of the consciousness of the words or sounds of speech that accompanies intensive thinking or reading. Authorities disagree as to the mechanism of inner speech. Some believe that it consists of a consciousness of the motor innervation of the muscles of speech; others, of a consciousness of the muscle and tendon

innervation; still others regard it as the consciousness of auditory sensations that proceed directly and, as it were, spontaneously from the auditory centers. Kern examined school children by giving them a short and simple text to read, and then questioned them as to the content. He found that the percentage of children who read with the accompaniment of visible movements of the lips or tongue was in inverse relation to the degree of intelligence. Among the most intelligent, the reading was entirely amotoric. Within these groups, the percentage of children who failed to comprehend the text was larger among the amotoric than among those who showed motor phenomena. Kern concludes that loud reading, whisper reading and silent or amotoric reading constitute a sequence that represents the normal development of human thought and reading. The younger the child and the lower the intelligence or the skill of the person the more the motor elements must be used in order to comprehend the contents of the text or to complete the thought mechanism. Kern concludes further that a clear enunciation is of great importance in teaching. He advises that the young child read aloud but that the older child be trained to silent reading. He calls attention to the importance of these observations in connection with disorders of speech. [It is interesting to recall the popular belief that adults who talk to themselves are of low intelligence.]

REICHLE, Cleveland.

ERGOSTERIN THERAPY IN MANIFEST SPASMOPHILIA. W. MANSBACHER, Ztschr. f. Kinderh. **46**:468 (Oct. 31) 1928.

Irradiated ergosterol preparations are suitable for the treatment of patients with spasmophilia, but good results are reached only by generous doses. In the clinical course of healing, first the open manifestations, then the electrical, and lastly the mechanical irritability disappear. The coexisting rickets takes the longest time to heal.

EMERSON, Boston.

THE RELATIONS BETWEEN TETANY AND WATER ECONOMY. H. BAAR, Ztschr. f. Kinderh. **46**:502 (Oct. 31) 1928.

A review of the present state of knowledge of the relations between salts and hyperexcitability leads to the conclusion that none of the hypotheses satisfy all of the facts. The researches here reported take as a working basis the view of Höber that irritability is a function of the state of imbibition of the tissue colloid. The addition of equivalent quantities of different salts to children with latent cases of tetany, whereby in some only the cation and in others only the anion is changed, results in a far reaching harmony between ionic activity, and position in the series of Hofmeister $Li < Na < K < Rb < Mg < Ca < Sr < Ba$. Potassium among the cations and phosphoric acid among the anions cannot remain in the series because of the strength of their action, and an attempt was made to get a clearer understanding of this deviation. The view of Höber, previously mentioned, establishes the fact that acids as well as alkalis, although by different concentration, may cause tetany. A series of known facts speak for the interdependence of the water content of the tissues and hyperirritability. Moreover, insulin has a tendency to cause tetany, and this tendency is brought into harmony with its action on the water economy; solution of pituitary acts similarly but more weakly, and a number of experiments are reported on the influence of diuretics on hyperirritability. The most unequivocal results were obtained with a brand of theophylline which in the majority of cases had such a favorable influence on tetany in infants that calcium chloride and ammonium chloride can be discarded as agents for combating tetany on the basis of symptoms. The increase of galvanic hyperirritability in a definite change of weather is reported, and an attempt is made to explain this phenomenon consistently as well as the peak for tetany in the spring.

EMERSON, Boston.

GROWTH IN LENGTH AND WEIGHT OF FEEBLEMINDED CHILDREN: II. A. ROSENBLÜTH, Ztschr. f. Kinderh. **46**:548 (Oct. 31) 1928.

The majority of feebleminded children are retarded in growth and in height; the minority show normal growth. Feebleminded children in institutions are more strongly influenced in relation to their growth, the retardation depending chiefly on the severity of the disease process. Among the idiots measured by the authors, a correspondingly greater retardation was found than among the patients with the mildest grade of feeblemindedness.

EMERSON, Boston.

THE CHEMISTRY OF THE CEREBROSPINAL FLUID. B. STEINER, Orvosi hetil. **72**:1265, 1928.

The content of inorganic phosphorus in the cerebrospinal fluid is between 1.4 and 1.6 mg. per hundred cubic centimeters. In meningitis, it is between 1.7 and 3 mg. In doubtful cases this increase of phosphorus content can be used for the diagnosis of meningitis. In tumor of the brain and acute encephalitis the phosphorus content of cerebrospinal fluid is decreased. The importance of determination of phosphorus lies in the fact that in the early stages the other methods usually are not quite reliable.

ZENTAY, St. Louis.

Diseases of the Eye

A CASE OF VACCINIFORM BLEPHARITIS DUE TO AN ATYPICAL HERPES VIRUS. H. B. ANDERVONT and J. S. FRIEDENWALD, Bull. Johns Hopkins Hosp. **42**:1 (Jan.) 1928.

Andervont and Friedenwald report a case of pustular eruption on the eyelids of a girl, aged 14, who had been successfully vaccinated for smallpox in early childhood. The lesions consisted of vesicles and pustules as large as 3 mm. in diameter, many of them umbilicated. *Staphylococcus albus* was obtained on culture from the lesions. This picture in no way suggested herpetic infection, and, except for the history of previous vaccination, would have been regarded as a typical example of accidental infection with vaccine virus.

From this patient a virus was obtained which when inoculated intracranially and on the scarified corneas of rabbits produced typical herpetic encephalitis and herpetic keratitis. Inclusion bodies were seen in sections from corneal epithelium, but not from the brains. Animals surviving infection from this virus were immune to typical strains of herpes virus. It is concluded that this virus is a strain of herpes virus.

LYTTLE, New York.

RETINITIS PIGMENTOSA ALBESCENS. BERNARD SCHLESINGER, Proc. Roy. Soc. Med. **22**:650 (March) 1929.

A case of retinitis pigmentosa albescens was reported in a girl, aged 9 years.

WILLIAMSON, New Orleans.

Diseases of the Ear, Nose and Throat

RETROPHARYNGEAL ABSCESS IN INFANTS AND CHILDREN. HARRY M. GREENWALD and CHARLES R. MESSELOFF, Am. J. M. Sc. **177**:767 (June) 1929.

The author reports an analysis of fifty-five cases of retropharyngeal abscesses in infants and children and states that this condition is not uncommon in early infancy and childhood and is more common during the first year of life than later. It occurs most frequently in winter and in spring when infection of the upper respiratory tract is common.

The author states that retropharyngeal abscess should be suspected in every case presenting enlarged cervical glands, and that a diagnosis should be determined

by digital examination of the pharynx. He points out the danger of operating when the patient has nonsuppurative lymphadenitis as well as the danger of not operating when fluctuation is present. The mortality rate in his series of cases was 7.3 per cent, demonstrating that even in the hands of experts there is a rather high mortality.

HENSKE, Omaha.

EFFICACY OF TONSILLECTOMY FOR THE REMOVAL OF FOCAL INFECTION. S. RHOADS and GEORGE F. DICK, J. A. M. A. **91**:1149 (Oct. 20) 1928.

The most frequent object in removing tonsils is to rid the body of tissue harboring bacteria capable of producing disease in other parts of the body. Incomplete removal of infected tonsillar tissue, even by specialists of established reputation, results in a failure to accomplish this, and occurs in 73 per cent of cases. Cultures taken from the "tonsil stumps" have considerable clinical significance since in a fairly large series in which cultures were taken, the "stumps" harbored more pathogenic bacteria per gram than did tonsils removed for the first time. Also, there are clinical cases in which patients with systemic diseases attributable to foci of infection failed to improve after the original tonsillectomy, but improved strikingly after removal of the "stumps." The complete removal of all tonsillar tissue is necessary when tonsillectomy is undertaken.

BONAR, Salt Lake City.

EAR INFECTIONS IN CHILDREN. J. A. MCASKILL, New York State J. Med. **29**:9 (Jan. 1) 1929.

The usual symptoms of mastoiditis may be absent in infections of the mastoid antrum, but gastro-intestinal and meningeal symptoms may be marked.

AIKMAN, Rochester, N. Y.

THE USE OF RADIUM IN DISEASED TONSILS. J. COLEMAN SCAL, New York State J. Med. **29**:65 (Jan. 15) 1929.

It is possible "to obtain a complete atrophy of the tonsils without producing any inflammatory reaction or injury to the surrounding structures," by the use of radium.

AIKMAN, Rochester, N. Y.

PAPILLOMATOSIS OF THE LARYNX AND TRACHEA. ARTHUR F. HOLDING, New York State J. Med. **29**:271 (March 1) 1929.

A child, aged 18 months, with dyspnea and cyanosis, proved to have laryngeal papillomas when examined with the bronchoscope. After five months' treatment, tracheotomy was performed. Papillomas were removed about once each month, and the child seemed to improve. After three years' observation, pulmonary edema developed, following bronchoscopic treatment, and the child died. At autopsy, papillomatosis was found not only in the larynx but extending down the trachea beyond the bifurcation; it was most marked around the tracheotomy wound. "The case illustrates the possibility of transplantation of the growth and stimulation of growth by chronic irritation."

AIKMAN, Rochester, N. Y.

FOREIGN BODIES IN THE ESOPHAGUS AND UPPER AIR PASSAGES. J. J. ROBB, Wisconsin M. J. **28**:258 (June) 1929.

The author urges more frequent use of roentgenography, fluoroscopy, esophagoscopy and bronchoscopy when the lodgment of foreign bodies is suspected. Twenty cases are reported, mostly in children under 6 years of age. Coins, peanuts and buttons were the most common objects found. Six patients had objects in the respiratory tract. One died while removal of a shoe button was being undertaken under chloroform anesthesia. Vomiting after taking solid foods was the most

common symptom when the object was in the esophagus, and spasms of coughing or choking when it was in the air passages. Foreign bodies should be removed, and not left in the hope that they will be coughed up.

JANNEY, Milwaukee.

RESORPTION OF BONE IN ACUTE MASTOIDITIS. JAN GORNY, Ztschr. f. Hals-, Nasen- u. Ohrenh. **22**:482 (Feb. 16) 1929.

In order to investigate the pathologic processes of lacunary bone resorption and to examine the nature of the osseous substances, the author studied splinters of bone histologically. He took a piece of the compact cortex and of the spongious region of the antrum. The specimens were put in formaldehyde, were decalcified in nitric acid and embedded in celloidin. The sections of a thickness of from 5 to 10 microns were stained with Mallory's hematoxylin. Specimens were taken from nine patients with developed skeletons. In inflammations of the mastoid process, following suppuration of the middle ear, bone cells were present which showed not only alteration but also changes that were progressive, in all probability. Single giant cells have been found in osseous lacuna. These giant cells probably developed from elements of the body substance proper. Howship's lacunae might develop from giant cells which migrate from the osseous substance into the soft parts. The physiologic metamorphosis in the osseous substance takes its course through the medium of osseous cells. It is improbable that these react only with alterative changes during the pathologic process leading to their destruction. Some of the phenomena cannot be explained in this manner. The osseous cells are osteogenically equal to the osteoblasts. When it is assumed that giant cells develop from the latter, the possibility cannot be denied that they develop from osseous cells. Changes of the osseous cells are found not only at the height of the resorptive process but at the beginning of the same. They can be found without the common signs of destruction in the form of giant cells or Howship's lacunae. The latter may be the final stage of the whole process. Herein lies, principally, the importance of the active participation of the osseous substance in lacunary resorption. In looking for early signs of mastoiditis, not only should the lacunary resorption be investigated but also the cells and the matrix. One may perhaps search here for the primary change of the bone in mastoiditis.

AMBERG, Detroit.

Diseases of the Skin

ETIOLOGY OF ALOPECIA AREATA. CARROLL S. WRIGHT, Arch. Dermat. & Syph. **19**:365 (March) 1929.

As evidence against the trophoneurotic theory of the cause of alopecia areata, a case is reported in which the sensory nerves that supply the scalp, the posterior root of the second cervical nerve and the entire supply of the sympathetic nervous system to the scalp were cut, to relieve the patient from the pain of an incurable cancer of the head and neck. This failed to produce alopecia areata or to affect the hair in any way.

The view that alopecia areata is a reaction phenomenon of irritation of the nerve roots from diseased teeth is questioned because, according to Head, reflex irritations from diseased teeth do not affect the scalp and because, if the view were true, a much greater incidence of alopecia areata would be expected, owing to the extreme prevalence of infections about the teeth. The author is led to suspect that a patchy fall of hair is due to interference with the vascular supply.

SHIRLEY, Iowa City.

HERPETIC INFECTION, WITH ESPECIAL REFERENCE TO INVOLVEMENT OF THE NERVOUS SYSTEM. ERNEST W. GOODPASTURE, Medicine **8**:225, 1929.

Herpes is a member of a large group of maladies of unknown etiology, manifesting itself in man, the lower vertebrates, insects, plants and perhaps bacteria. It is probably caused by a filtrable virus.

In spite of the discovery of etiologic agents belonging to the bacteria and protozoon groups, specific for certain diseases, "there remains the important group of filtrable virus diseases which appear to be infectious, and are often the most contagious of diseases, where causative agents have neither been cultivated on lifeless media nor yet identified with certainty by means of the microscope." These viruses are known only through the changes which they induce in certain cells of the host.

Two views concerning the filtrable viruses are: (1) they are extremely small living parasites, too small for detection by the present method, and (2) they are nonliving agents of the nature of enzymes. These ferments (toxic substances) cause certain cells to reproduce the specific virus.

There is no doubt that certain viruses have been proved specific for certain diseases. It has recently been shown that the herpetic virus, which causes the common fever blister or cold sore of the lip, is also neurotrophic, and it is now classified with the viruses of rabies and acute anterior poliomyelitis. In some animals (the rabbit), in fact, the herpetic virus is more virulent than either rabies or poliomyelitis in man. Many strains of herpetic virus, implanted on the mucous membrane or on the skin of the rabbit, are capable of inducing a rapidly fatal disease of the brain or the spinal cord.

In 1912, Grüter demonstrated that material from a herpetic blister, if inoculated into rabbits, will cause herpes and that a series of inoculations can be transmitted. This work helps in the understanding of the herpetic infections in man and aids the interpretation of the activity of other viruses.

A study is made to consider the relationship, if any exists, of herpes simplex to herpes zoster, and to epidemic (lethargic) encephalitis. A sharp distinction must be made between zoster and herpes simplex. Zoster is not transmissible to animals and is at present apparently not infectious.

The symptomatology of various forms of herpes is discussed and the various locations described. Some herpetic eruptions seem to be idiopathic; that is, they are not associated with any other pathologic condition. Some are symptomatic or secondary to another condition. Various infectious diseases are noted for herpetic lesions, which usually occur at the mucocutaneous line of the lips. Certain chemical irritants may produce similar lesions.

In the course of many experiments, inoculations have been made on rabbits, notably on the cornea. In some instances, the result is limited to the site of scarification. In other cases there have been marked systemic manifestations, while in still others the central nervous system has been involved. It is supposed (Daeor and Schnabel) that, since involvement of the central nervous system may follow inoculation of the blood stream, the virus gains access to the brain through the vessels of the eye. Levaditi maintained that the transmission is from the cornea along the line of the optic nerve to the brain. Friedenwald suggested that the central nervous system was invaded by way of the sensory division of the fifth nerve, after finding active virus in the gasserian ganglion. This suggestion has been justified by the experiments of Goodpasture and Teague.

Following superficial implantation, any mucous or serous membrane or almost any viscus can become affected. It has also been shown that peripheral nerves, whether sensory, motor or sympathetic, may serve as portals of entry into the central nervous system. This is experimental work and some of the results are extremely artificial, i.e., hardly liable to occur in ordinary infections. Goodpasture found, however, that normal rabbits which were placed in the same cage with rabbits having corneal herpes soon became infected with encephalitis. This invasion occurred along the sensory division of the fifth nerve. The mucous membrane of the throat and mouth seems to be the most vulnerable and, it is concluded, is the route through which the encephalitis of man, incident to herpes labialis, occurs.

While some observers have apparently demonstrated a virus indistinguishable from that of herpes in the brain or spinal fluid in certain cases of encephalitis

in man, other workers have failed in this effort after repeated attempts. Such an accomplishment must be regarded as exceedingly rare; much yet remains to demonstrate the connection.

The author states that "The problem of the etiology of epidemic encephalitis is still unsolved, and at the present time there does not seem to me to be any convincing evidence that it is caused by the herpetic virus."

ROYSTER, University, Va.

THALLIUM MEDICATION IN TINEA CAPITIS AND OTHER DERMATOSES REQUIRING EPILATION. E. WILLIAM ABRAMOWITZ, New York State J. Med. **29**:253 (March 1) 1929.

The treatment in eighteen cases of tinea capitis and in one case of favus is reported; 8 mg. of thallium acetate per kilogram of body weight gave good results.

Thallium should not be used after puberty, or for children who are in poor health, underweight or affected with albuminuria. AIKMAN, Rochester, N. Y.

WATER METABOLISM IN INFANTILE ECZEMA. L. RIBADEAU, M. LEVY and S. MIGNON, Nourrisson **17**:65 (March) 1929.

Application of the Aldrich-McClure intracutaneous saline test in infants with eczema showed a diminished absorption time varying from nine to forty-five minutes. One case of slight eczema showed the normal time, namely, sixty minutes. Studies on the water content of the blood plasma revealed the presence of moderate hydremia in some cases and a normal water content in the others. A lowering of the albumin-globulin ratio of the plasma was also found in a majority of the cases. This was associated with a lowering of the serum protein content similar to that in cases of nephrosis. McCLELLAND, Cleveland.

PROTEIN CONTENT OF THE PLASMA IN CASES OF INFANTILE ECZEMA. ERNA LEVY, Nourrisson **17**:71 (March) 1929.

Chemical studies of the nitrogen content of the blood serum were made in normal infants and in infants with eczema. Calculations showed that the serum protein of normal infants increases from 5.5 to 7.5 per cent during the first year. The eczematous infants frequently showed a hypoproteinemia, but this was not a constant observation as several had normal values. The lowest figure was 3.6 per cent. Infants with weeping eczema of long duration usually showed the lowest amount of serum protein. Relief from the eczema was accompanied by an increase of serum protein. Studies in basal metabolism failed to show any nitrogen unbalance. The author advances the theory that excessive exudation of serum from the skin lesions may account for the decrease in protein in the serum. On this hypothesis, she advises a diet sufficient to compensate for the excessive loss.

McCLELLAND, Cleveland.

IMPETIGO BULLOSA; REPORT OF CASE. M. DA ROCHA, JR., Arch. de pediat., Rio de Janeiro **8**:265 (May) 1929.

A child, aged 9 months, developed generalized bullae following influenza. The treatment consisted of mild antiseptic solutions, followed by glycerite of boroglycerin, U. S. P. The child recovered in fifteen days. SANFORD, Chicago.

THE INHERITANCE OF ICTHYOSIS CONGENITA AND ICTHYOSIS VULGARIS: V. HEREDITY. HERBERT OREL, Ztschr. f. Kinderh. **47**:312 (March 23) 1929.

Icthyosis vulgaris and icthyosis congenita are different in their course of inheritance and are two anomalies which must be sharply differentiated (Siemens and Leven). There are cases of icthyosis congenita which, on account of the

mildness of the signs, are to be reckoned as transitional forms of icthyosis vulgaris; there are also cases in which icthyosis congenita later resembles icthyosis vulgaris in high degree: cases reported by Hallopeau and Waterlet, cases 1 and 2 of Siemens, and case 5 of Orel. It is not known on what the difference between the two anomalies depends in the last analysis. At present one can only classify and register the individual cases and similar observations of the families. Not only the cases of icthyosis congenita and of icthyosis vulgaris must be separated, however; one must go still further and try to differentiate the individual cases of icthyosis vulgaris according to the kind of inheritance; if they are alike in the acquired sense, they cannot possibly be alike in the sense of inheritance, for some patients inherit the characteristic as dominant, others as recessive, and in each instance it is limited to the same sex. Perhaps later, clinical and histologic differences can be found if the circumstances of inheritance are observed accurately. The question is a weighty one as to whether icthyosis vulgaris is inherited simply as a recessive characteristic. As to this, further familial, biologic researches are needed, especially in those families with normal parents whose children of different sex have icthyosis. If more frequent blood relationships are found in these parents than correspond to the average, then the recessive course of inheritance would be shown.

EMERSON, Boston.

PROGERIA BEGINNING WITH EXTENSIVE SCLERODERMA; REPORT OF CASE. F. STRUNZ, Ztschr. f. Kinderh. **47**:401 (March 23) 1929.

A child in whom Kneschke reported true scleroderma at the age of 4½ months is reported by Strunz, who observed her while she was both in and out of the hospital up to the age of 4½ years and described her condition as severe general disease corresponding to the picture of progeria described by Gilford. As the girl became older, the original red cell count of 6.7 millions diminished to 4.2 millions. The skin on the legs became normal, although the knees could not be completely extended because of stiffness, and the skin on the abdomen remained affected. In general, not only the hardness and tenseness disappeared, with atrophy in some spots, so that the skin could be folded, but also the redness, for the most part, which left some pigmentation and itching. The muscle under the diseased skin showed delayed development and was atrophic. The great retardation in the growth of the bone system was manifested by considerable kyphosis, by the small pelvis, and by the fact that the anterior fontanel showed an opening of 1 cm. and that the orbits were small enough to cause exophthalmos; all these conditions existed, while the patient had no signs of rickets and had good teeth. The child had a birdlike face, with an atrophic, bald head, a thin, sharp nose, protruding eyes and a small, retreating chin. The other charatceristics were a clear, shrill voice, a good mental development, a poor appetite and freedom from intercurrent disease during the entire time. In one case in the literature, reported by Kraus, the condition was congenital. The great majority of observers (fifty-eight) look on the thyroid gland as the cause of the disturbance, but Strunz suspects the hypophysis on the grounds of the general disturbance of growth in the bones; this child showed dwarfism, the open fontanel, the gaping sagittal suture, the lines 1.5 cm. above the epiphyses visible in the roentgenogram of the lower and upper part of the legs, as well as the pointed and atrophic phalanges, the narrow width of the sella turcica, the much retarded pelvic girdle, the polyglobia, the birdlike face and a slight but definite Abderhalden's reaction, all signifying a condition of acromicria, the opposite of acromegaly. There was no abnormal distribution of fat or hypoplasia of the genitalia, and no diabetes insipidus. A close relation of the endocrine organs and the autonomic nervous system, spoken of by Hoffman, was tested by the method of Eppinger and Hess; in regard to hyperirritability of the vagus, only a slight deviation from the normal was found, although there was a definite response of the pulse and the blood pressure to doses of atropine and pilocarpine which are inactive in normal children. In these experiments it seemed probable that the disturbance was due to a hypofunction of the anterior lobe of

the hypophysis, and also in some degree to the vegetative nervous system, in the sense of a hypertonia of the parasympathetic and hypotonia of the sympathetic component.

EMERSON, Boston.

Surgery and Orthopedics

SYMPATHETIC RAMISECTION IN SPASTIC PARALYSIS. H. LEROY VON LACKUM, J. A. M. A. **92**:139 (Jan. 12) 1929.

Sympathetic ramisection is the most effective means of relief in many cases of spastic paralysis, although the operation is still judged on an empiric basis, since basic knowledge of muscle tone and the rôle played by the sympathetic is still lacking. The best results can be obtained only in patients with good mentality, and in those in whom there is no block in the will to move. Treatment for contractions can be avoided if the patients are treated early.

BONAR, Salt Lake City.

INFANT CIRCUMCISION. WILLIAM B. D. VAN AUKEN, New York State J. Med. **29**:82 (Jan. 15) 1929.

The author gives a discussion of the indications, contraindications, objections, age for operation, technic and complications of circumcision.

AIKMAN, Rochester, N. Y.

ACUTE OSTEOMYELITIS AND COMPLICATIONS. N. D. BITTING, South M. J. **22**:580 (June) 1929.

Diagnosis within the first forty-eight hours, followed by prompt surgical intervention, will greatly lessen the time of hospitalization, the morbidity and the deformity.

Positive roentgen observations will not be obtained during the first forty-eight hours. In all cases accompanied by a severe bacteremia the patients will obtain the most benefit from repeated blood transfusions as an aid to the surgical treatment. After drainage of pus has been established, proper immobilization of the limb should be carried out to prevent fracture and deformity.

SCHLUTZ, Minneapolis.

OSTEOMYELITIS. HAROLD EDWARDS, Practitioner **122**:209 (May) 1929.

Pyogenic diseases of the bone fall into two groups, open and closed. The former cases are usually compound fractures and the infection is usually mild, as the products of bacterial growth escape through the open wound and are not absorbed. In closed infections, the organisms may reach the bone by direct extension from an adjacent septic focus or by way of the blood stream. Examples of the former are acute mastoiditis and alveolar abscess.

Infection through the blood stream demands the closest study. The disease is one of childhood, with a greater incidence in boys. The tibia, femur and humerus are the bones most frequently affected. The diaphyseal side of the epiphyseal line is almost constantly the site of commencement of the disease.

Two theories are in evidence to explain this incidence: (1) the injury to the less resistant cancellous bone beneath the epiphysis, and (2) the vascular theory. Repeated attempts have been made to show that the terminal branches of the nutrient arteries are end arteries.

In the fulminating type, the lesion is solely a local manifestation of a general septicemia. The intense toxemia may so obscure the local lesion that diagnosis is delayed, a fact that militates against the chances of recovery. In the ordinary type, with localizing signs and symptoms, tenderness through the entire length of the bone on percussion is a helpful diagnostic sign. In the mild acute type, the course is longer and the signs much less marked. In a certain number of cases the condition is chronic from the first and never enters into an acute phase.

All persistent mild pains in the bones of children call for roentgen examination.

The difficulty of adequate drainage is great because of the structure of bone. There are three methods open to the surgeon: (1) excision of the diseased bone and the formation of a gutter, (2) excision of the diaphysis with a bone graft at a later date and (3) draining the medulla through a series of drill holes through the cortex.

The fulminating cases are almost invariably fatal. The younger the patient is, the worse the prognosis. There is always the possibility of a recurrence.

BARRETT, San Francisco.

OPERATION FOR INGUINAL HERNIA IN THE CHILD. H. SALZER, Wien. klin. Wchnschr. **42**:674 (May 16) 1929.

The author presents a lecture based on his experience. He regards inguinal hernia in infants as always congenital. Unless the hernia interferes with development or becomes strangulated, operation should be deferred until after the tenth month of life, and then invariably performed. Trusses are never advisable. Hydrocele of the cord, but not of the tunica vaginalis, and undescended testicle always require operation.

CLAUSEN, Rochester, N. Y.

INTESTINAL OCCLUSION OF COMPLEX ORIGIN. M. FEVRE, Arch. d. mal. de l'app. digestif **19**:291 (March) 1929.

The author reports a case of multiple intestinal occlusions in a child, aged 6 years. Three different occlusions of the intestinal tract were found at operation. There was an occlusion in the jejunum caused by a ligament, an intussusception of the ileum and retrocecal herniation of the lower small intestines. The first two forms are rather common; the third is not seen often and in this case was due to an increased mobility of the colon. This condition particularly predisposes to herniation if the cecum is caught in a parietal scar as in this patient, in whom an operation had previously been performed on the appendix.

ZENTAY, St. Louis.

STRANGULATED HERNIA IN EARLY INFANCY. A. MARTINEZ VARGAS, Med. de los niños **30**:97 (April) 1929.

In one year the author had four cases of strangulated hernia, the oldest patient being a boy, aged 8 months. He expresses his belief that the condition is not as infrequent as is generally thought. The constriction in the majority of cases is caused by the external inguinal ring. Care must be exercised in differentiating between hernia and abscess of the inguinal region, undescended testicle and congenital hydrocele. There is a characteristic gurgling sound in strangulated hernia that helps in the differential diagnosis.

DWYER, Kansas City, Mo.

INTUSSUSCEPTION IN AN INFANT AGED SIX MONTHS. E. SKIPIRZEPA, Pediatria Polska **9**:49 (Jan. and Feb.) 1929.

An infant, aged 6 months, was operated on within twenty-four hours after intussusception occurred, with resulting recovery.

KRUPINSKI, Chicago.

Miscellaneous

PROPER SHOEING OF THE CHILD. JOHN D. ADAMS, J. A. M. A. **92**:1753 (May 25) 1929.

Seven vital and essential points should be incorporated in an ideal shoe: (1) The toes should be uncompressed in the shoe; (2) the shoe should be at least one-half inch longer than the weight-bearing foot; (3) the moccasin toe and the turned shoe give the proper depth and fullness for the toe; (4) a close-fitting,

well shaped heel, tapering at the top to fit the natural conformation of the os calcis is necessary; (5) depth and fulness in the line running from the anterior fold of the ankle to the base of the toes are necessary; there must be a lack of constriction at this point to allow a proper bearing and leverage of the toes; (6)the sole should be broad and flexible, with a straight outside bearing from the tip of the little toe to the width of the heel, since the weight should fall on the straight outside of the foot; (7) for children up to 3½ years of age, the heel should be no thicker than the sole, and in those from 3½ to 5 years it should be twice as thick.

BONAR, Salt Lake City.

UNERUPTED TEETH. WILLIAM LINTZ, M. J. & Rec. **129**:670 (June) 1929.

All teeth may fail to erupt. In the author's study, the frequency of unerupted teeth was from 0.4 to 0.8 per cent, the tooth most commonly unerupted being the upper lateral incisor in the female; endocrine stigmas were a marked feature, especially thyroid and gonadal disturbances, and harelip and clept palate did not necessarily occur in the offspring of a mother with unerupted lateral incisors. Infection and suppuration of deciduous teeth may destroy the buds of the permanent teeth. In children with an unerupted tooth, other anomalies are frequently found. The author states his belief that an unerupted tooth is merely another anomaly.

WILLIAMSON, New Orleans.

THE UNDER-NOURISHED CHILD: ANALYSIS OF RESULTS OF CONVALESCENT CARE. T. S. WILDER, New England J. Med. **200**:634 (March 28) 1929.

The study covers 287 medical cases of patients admitted consecutively to the Convalescent Home, Wellesly Hills, Mass; 97 per cent of this group gained weight after admission; of the remaining 3 per cent (8 children) details indicate that the average losses were insignificant, the children were only slightly underweight and their average stay (ten days) was probably too short.

There were 151 children who, without presenting gross evidence of any disease, showed marked underweight, ranging from 8.5 to 11.3 per cent; their average gains lay between 11 and 19 ounces (311 and 538 Gm.) a week, and they added from 7.5 to 10 per cent to their weight on admission. Their average stay was between twenty-five and thirty-five days, the tendency being for the older group of children to stay longer; the majority of the undernourished children were between 5 and 10 years of age, and between 35 and 65 pounds (15.8 and 29.4 Kg.) in weight.

In nearly all cases the principal gain occurred in the first week, with a large gain also in the second week, after which there was a rapid falling off in rate as normal weight was approached. Judged from the seasonal standpoint, the rates of gain over a period of ten weeks were: spring, 16.3 per cent; summer, 17.4 per cent; autumn, 21.8 per cent, and winter, 22 per cent. Since the report of Clough and Murlin showed that the most rapid gain in height occurs in the spring and the early summer, the author suggests that a child first makes a sudden advance in height in the spring, and then puts on weight, in proportion, in the autumn and winter, after the usual greater activity during the summer has passed.

There were the usual number of relapses after the children left the institution, and the author says, "Consequently, it does not appear advisable to invalidize a child in order to make him normal in weight, unless one also takes pains to correct the unfavorable influences in his environment which so often are to blame."

GENGENBACH, Denver.

EXCESSIVE CRYING IN YOUNG INFANTS. A. G. ALARCON, Nourrisson **17**:77 (March) 1929.

The author does not subscribe to the opinion advanced by Sisto (Buenos Aires) that excessive crying in young infants is usually a manifestation of congenital syphilis which gives rise to pain in the bones. A more satisfactory explanation

for excessive crying in infants under the age of 3 months is that they are suffering from vagotonia. The generalized hypertonicity of these infants offers supporting evidence. A therapeutic test consists of the administration of atropine which counteracts the increased muscular tone and tranquilizes the patient. Some cases in which the condition is unaffected by atropine and which last longer than three months are due to congenital syphilis, which probably prevents the proper development of the pyramidal tracts. The author states his belief that incompletely developed pyramidal tracts prevent the inhibiting stimuli from the cerebral cortex from reaching the voluntary and involuntary muscular systems.

McCLELLAND, Cleveland.

ACCIDENTS IN ULTRAVIOLET THERAPY. S. DELAPLACE, Paris méd. **16**:381 (April 20) 1929.

Delaplace divides these accidents into three groups. The immediate accidents are those due to trouble with the lamp. The principal difficulty is the detachment of an electrode in the mercury vapor type of lamp or of a carbon in the carbon arc type, causing severe burns. Other accidents of this sort are the development of excessive heat in the carbon type of lamp and an explosion in the mercury vapor lamps. Another cause of trouble is the susceptibility of some women to ozone, or the poor ventilation in lamps in which excessive heat is generated. The second group, or secondary accidents, are those due to injuries to the eye or to excessive erythema. The third group, or late accidents, are those due to the lessening of resistance to general infections after an intensive course of ultraviolet therapy. This applies especially to young infants suffering from tuberculosis or from diseases of the lungs. In adults, the resistance to contagious disease may be lessened.

SANFORD, Chicago.

THE USE OF CALF SERUM IN PEDIATRICS. G. POUCHET-SOUFFLAND, Progrès méd. **23**:997 (June 8) 1929.

The serum was used in fifty cases, including those of rickets, adenopathy, failure to gain and infections. It was taken by mouth. In all cases, satisfactory results were obtained: There was a gain in weight, the appetite was increased and irritability overcome. In seventeen cases of suppuration, the infections cleared up much more rapidly than was usual under ordinary medication.

SANFORD, Chicago.

INTERNATIONAL CONGRESS FOR THE PROTECTION OF INFANCY. JOSE VELASCO PAJARES, Med. de los niños **30**:104 (April) 1929.

At a meeting held in Paris in July, 1928, representatives from England, France and Spain discussed measures for the protection of child life. Among the measures advocated were: (1) the necessity for subsidizing the working mothers so that they would be able to nurse their infants; (2) the organization of "crèches" or nursing rooms for the infants of working mothers; (3) the teaching of puericulture in normal schools, and (4) the establishment of more open air schools.

DWYER, Kansas City, Mo.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Forty-First Annual Meeting, May 20-22, 1929

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Third Session, May 21, 9: 15 a. m.

THE DIAGNOSIS OF TUBERCULOSIS OF THE TRACHEOBRONCHIAL GLAND WITH ANATOMIC CONTROL. DR. P. F. ARMAND-DELILLE.

The necessity of all physicians recognizing the presence of tuberculosis of the hilum and bronchial glands at the earliest possible date is stressed. Even though it may mean a shorter or longer stay in a preventorium, the dangers run far outweigh the inconveniences.

Unfortunately, the physical signs and symptoms are inconclusive. Many children who are not infected have a delicate appearance, a certain number will have a prolonged fever from a cause other than tuberculosis, and too often the location of the infected glands themselves makes it impossible for many time honored but doubtful physical diagnostic measures to lend much aid.

An attempt was made in this study to correlate the roentgen manifestations with the actual condition found at necropsy by means of anatomic control.

These observations make it seem clear why dulness is often not found and why the d'Espine and other signs fail.

The cutaneous tests and a properly conducted roentgenologic approach are invaluable. Not only must direct anteroposterior plates be taken, but direct lateral views are just as essential.

As proved by the series of anatomically controlled x-ray plates, many of the diseased glands, some of which are extensive in size, could never have been detected without a direct lateral exposure.

THE GROWTH OF THE HUMAN VASCULAR SYSTEM: A QUANTITATIVE STUDY, WITH SOME FUNCTIONAL IMPLICATIONS. DR. RICHARD E. SCAMMON.

The ponderal growth of the heart in prenatal life is somewhat different from that of the body as a whole or of other organs of the body. Starting in early fetal life with a slow rate of growth, the organ enters a period of rapid increment in the later part of fetal life and at birth has reached a relatively large size. This increased growth of the heart in later fetal life is probably associated with the growth of the vascular bed of the placenta.

During the first trimester following birth, the growth of the heart is almost at a standstill. This is shown by data on the weight and dimensions of the heart taken at autopsy and by measurements of roentgenograms of the heart. This quiescent period in growth of the heart is attributed to the loss at birth of the vascular bed of the placenta.

Following the quiescent period of early infancy, the heart grows in somewhat the same fashion as the body and most of the larger viscera do and shows the same general phases of increment.

It has been possible to develop analytic expressions for the weight of the heart with respect to age or time in the first two decades, and the absolute and relative rates of growth of the organ have been worked out from these expressions. The absolute rate of cardiac growth rises rapidly during fetal life and reaches its maximum for the entire growing period at the time of birth. The rate then

declines to a minimum at about six years. Following this decline is a rise to a second, although smaller, maximum at puberty. During adolescence, there is another decline in growth rate.

The relative rate of cardiac growth is at its maximum in early fetal life. It declines rapidly until about a year after birth and then more slowly for six years. Thereafter, there is a small secondary rise reaching its peak before puberty at about nine years. After this time, the relative rate declines. The secondary peak of growth prior to puberty is perhaps associated with the rapid development of musculature at this time.

The absolute variability in the weight of the heart increases at a fairly steady rate throughout the developmental period, although not as rapidly as does the heart weight itself. In the adult the heart weight is approximately eight times as variable (in absolute amounts) as in the young infant.

DR. L. R. DEBUYS: One thing that came to my mind in the early part of Dr. Scammon's presentation was: In the study of the heart in fetal life, comparisons were made between the weight of the heart and the length of the fetus; after birth, the comparisons were made between the weight of the heart and the age of the person, and certain variations at different ages are mentioned.

I was wondering whether these variations at the different ages were influenced by the height of the person. The reason for my asking this question is that not infrequently, when roentgen observations are made, the report comes back that the heart is enlarged. Might not the heart be larger in a person who is taller for his age?

Of course there are many interesting factors to consider in the interpretation of the roentgen picture; for example: the type of the heart, the type of the chest, the period in the cycle of the heart at which the roentgenogram is taken, and others.

DR. ISAAC A. ABT, Chicago: The older clinicians, among whom may be mentioned Rauchfuss, Baginsky and Soltmann, stated that at puberty the heart increased and that the vascular bed diminished in size. They stressed the point, too, that at this time of life patients with cardiac disease usually became worse and in many of them decompensation occurred.

I should like to ask Dr. Scammon if that statement remains true, or if there was any foundation in fact for the statement which was made fifty years ago.

DR. RICHARD E. SCAMMON: With regard to the change in length, we plot against length in prenatal life. If we plot heart weight against body length in postnatal life we will get essentially the same curve I have shown in age, because length and age are probably more closely related than almost any other physical measure. So if this is reduced to length, this curve will be seen again.

The reason we do not plot against length in postnatal life is because we have difficulty in getting length. We can get 10,000 in regard to time and only 2,000 in regard to length. But it is essentially the same relationship because of close linking of age and body length in a large group of cases. They are extremely closely related, in fact, closer, I believe, than with time.

With regard to the changes at puberty, there have been some recent measurements made on the vessels, particularly on arteries. The reason people thought the arteries were somewhat reduced was because they were comparing them with the veins.

There is a tremendous growth of veins at the time of puberty, and I think that people made the comparisons of veins and arteries and thought that the arteries were much smaller as compared to venous return.

I would say that immediately preceding puberty there is a change in the heart, that the heart is growing rapidly and has a high degree of variability. This is a period when growth is going on rapidly, and the great variability represents the varying way in which the organisms respond to that period of growth. When there is a rapid period of growth, it commences to scatter and is reflected in the variability. I think the variability does have a connection with the point that Dr. Abt brought out.

The relative size of the heart, however, remains essentially the same so far as we can determine. We do not find any evidence, such as the old observers did, that there is a change in the heart with respect to body weight. That relationship, so far as we can see, is not essentially modified by this rapid growth which precedes puberty and reaches its apex after puberty.

METABOLIC STUDIES ON NEPHROSIS WITH PARTICULAR REFERENCE TO NITROGEN BALANCE. DR. D. M. COWIE, DR. KATHARINE M. JARVIS and DR. MOSES COOPERSTOCK, with the technical assistance of DR. ASA NAKAO.

A case of chronic glomerular nephritis in which the condition had passed into the nephrotic subgroup of glomerular nephritis during the patient's first four months' stay in the hospital is recorded. Edema disappeared toward the end of a four months' stay in the hospital and continued for more than a month before observations on metabolism were begun. The metabolic observations extended over 105 days. This time was divided into four periods. During the first period of twenty days, adequate protein intake was continued (45.4 Gm. per day). The patient remained free from edema and showed a marked positive nitrogen balance. The urinary albumin varied from 3 to 4 Gm. per day. During the second period of twenty-five days, the protein intake was lowered to 25.4 Gm. The patient quickly showed a negative nitrogen balance which was recorded seven times during the period. Edema and ascites began to develop promptly. During the third period, a still lower protein intake was given, 17.9 Gm. The nitrogen balance was more often negative. The edema more than doubled its previous degree. During the fourth period, a high protein intake, 70 Gm. a day, was given. A quick high positive nitrogen balance immediately occurred. The edema continued to increase for three days, and then suddenly and completely disappeared. In five days there was a loss of 9 pounds (4.1 Kg.) in weight. This condition continued until the patient was discharged from the hospital twenty-six days later.

A high protein intake brought about an increase of about 150 per cent in the urinary albumin output for the first fifteen days of the period of the highest protein intake. There was then a quick adjustment of the urinary albumin to a much lower level, but it was still 56 per cent above the average for the previous periods. An average amount of protein for the growing needs of the body was necessary to keep the urinary albumin at the lowest level. If the intake was raised or lowered from this point, the urinary albumin increased.

Frequent determinations of nonprotein nitrogen were done. The average was 28.1, the lowest 20.7, the highest 37.9. From these figures it is safe to say that the retained nitrogen in the two stages of marked positive nitrogen balance was not held in the circulating blood. The nonprotein nitrogen of the ascitic fluid during a time of marked ascites was 14.2. It is our belief that the retained nitrogen is retained in protein storehouses.

There seems to be a definite relationship of serum protein to edema. A serum protein below 4 with reversed albumin-globulin ratio is not incompatible with the absence of edema, while a serum protein above 5 is never associated with edema. The albumin-globulin ratio in our case went as low as 0.24.

The serum protein of the blood was consistently highest during the periods of adequate and high protein feeding.

In our case, edema cannot be ascribed to a lower osmotic pressure of the blood. The chlorides were almost invariably above normal. There was no consistent increase in the ascitic chlorides. The organic crystalloids were normal. The salt and crystalloid content of the blood offset the loss of colloid.

The cholesterol remained high throughout the entire study. It seemed gradually to increase during the first period of edema and reached its highest point, 704, during the second period of edema. It continued high, however, through the last edema-free period.

The basal metabolic rate was consistently high throughout the 105 days— +20, +19, +22, +21, +23 and +13. In this respect, our case differs from the usual one of its kind.

DISCUSSION

DR. BENJAMIN KRAMER, Brooklyn, N. Y.: There are two points I would like to stress in connection with the relationship of the calcium concentration to the protein of the serum. If I understood correctly, Dr. Cowie stated that in his patient the serum calcium was normal, although the serum protein concentration was only 4 per cent. This is unusual for such patients, because from 30 to 50 per cent of the calcium is bound to protein.

A reduction of serum protein would be accompanied by a diminution of about 0.6 mg. of calcium for each 1 per cent reduction in serum protein.

In some studies of cases of nephrosis, Dr. Pincus and I confirmed this observation and showed that the reduction is in the nonultrafiltrable fraction of the serum calcium.

I should like to ask Dr. Cowie whether he found this relationship of increased protein intake to disappearance of edema a common phenomenon, or rather an unusual manifestation in this particular patient. I have been unable to influence the edema by giving a diet high in protein content. The administration of huge doses of thyroid substance to one patient seemed to have a definite effect on the edema. As much as 20 or 30 grains (1.3 or 1.95 Gm.) of thyroid extract was given a day. In spite of this enormous dose, the basal metabolic rate did not seem to be measurably affected.

DR. D. M. COWIE, Ann Arbor, Mich.: I stated that the calcium was normal at the beginning of the period. I did not wish to go into the question of calcium variations (which, however, in this case were always within the normal range or lower). I particularly wished to emphasize the point that we were describing only one case which seemed to be worth recording because we had followed its transition through the preliminary manifestations of a glomerular nephritis. If this patient had come to us later, at a time beyond the presence of casts and blood in the urine, we might have thought that the condition was so-called pure nephrosis, not dependent on nor associated with a kidney lesion. It seems a rather good illustration of a case of nephrosis at the stage in which the kidney was involved and which then passed into a stage in which we are unable to find any evidence of kidney disturbance as indicated by casts, blood, etc.

We have had cases similar to those Dr. Kramer spoke of. We had one case which came to autopsy. It is surprising that we found practically no characteristic nephritic changes in the kidneys; yet it was as marked a case of so-called nephrosis as the one we have just presented, and at one time the urine showed blood and casts.

With regard to thyroid extract, we have treated patients with nephrosis with thyroid and have had the same experience Dr. Kramer describes. We have had still other cases in which a high protein diet did not bring about the marked effects seen in this case. I am not familiar with the idea that a high protein diet raises the calcium content of the blood. (We have considered calcium variations between 9.5 and 12 as normal.)

THE INTERMEDIATE PROGNOSIS OF ACUTE NEPHRITIS IN CHILDREN. DR. JOHN D. LYTTLE.

This work on nephritis in children was begun by Dr. Wilcox in 1921, and the material consists of reports of the cases on the pediatric service at Bellevue Hospital for the past seven years. The figures are based on a follow-up study of patients from 1 to 7 years of age. I have excluded all cases of syphilitic, purulent and chemical nephritis, so-called febrile albuminuria and the focal nephritis that occurs in endocarditis. The cases are grouped according to the classification in use today, i. e., glomerular, tubular and diffuse glomerulotubular nephritis. I will say at once that damage to the kidney is never limited to one part of the kidney structure; all the cases show mixed nephritis. But in those cases called glomerular, the clinical and anatomic observations point to a minimal tubular change and in those called tubular the observations indicate a minimal glomerular change.

Criteria for Classification

	Glomerular	*Tubular*
Edema	Moderate (hard)	Massive (soft)
Blood Pressure	Increased	Normal
Uremia	Frequent (13 per cent left) (41 per cent bilateral)	Rare
Urine	Bloody	Yellow
Albumin	Moderate	Massive
Nitrogen Retention	Common	Rare
Serum Protein	Normal	Low
Cholesterol	Normal	High

Hematuria and hypertension are the features of glomerular nephritis, while generalized edema, massive albuminuria and normal blood pressure are characteristic of tubular nephritis.

The term diffuse is used here to mean a mixed glomerulotubular nephritis. If a patient with bloody urine, hypertension and nitrogen retention showed a marked edema and albuminuria, with low serum protein and high cholesterol content, the nephritis was called diffuse, or if a patient with massive edema and albuminuria, low serum protein and high cholesterol content had gross hematuria, persistent hypertension or nitrogen retention, the nephritis was also called diffuse.

Strictly speaking, the six cases of tubular nephritis could be put in the group of diffuse nephritis. All of them showed slight clinical evidence of glomerular involvement, and in the two cases that came to autopsy, there was definite evidence of glomerular damage.

The pure nephrosis described by Epstein and others and attributed to a disturbance of metabolism of protein and fat, in which the renal change is only one manifestation of a generalized metabolic disease, I have never seen in a child. But if by nephrosis is meant nephritis in which the clinical and anatomic evidence shows little glomerular inflammation, then the six cases I have called tubular nephritis might be called nephrosis.

Prognosis.—I can say nothing about the ultimate prognosis of these cases at this time. What I am concerned with now is the immediate and intermediate prognosis based on follow-up work for from one to seven years after the acute nephritis.

The table presented here shows the basis used for classification.

Without going into the etiology too much, I think that the chart showing the seasonal incidence in these cases of acute nephritis and the seasonal incidence of infections with the hemolytic streptococcus at the Presbyterian Hospital for one year is of interest. About 66 per cent of our cases occur in the four months from January to May. The incidence of infections with the hemolytic streptococcus closely parallels the incidence of acute nephritis.

The next table (not presented here) shows the recent infections in these cases. By recent is meant within three weeks before the onset of the nephritis. Ninety-five per cent of the patients with glomerular nephritis, all of those with tubular nephritis and 77 per cent of those with diffuse nephritis gave a definite history of recent infections.

Table 3 (not presented here) shows the intermediate prognosis in these cases. The total mortality for the group is 9 per cent, and of the fifty-six cases followed in nine, or 16 per cent, the condition became chronic. There were 4 deaths in the glomerular group, a mortality of 5.4 per cent, as compared to a mortality of 50 per cent in tubular and 11.7 per cent in diffuse nephritis. Of the four deaths from glomerular nephritis two were due to uremia, one to hemolytic streptococcus septicemia and one to pneumonia. Two of the three deaths in the tubular group were due to pneumococcus peritonitis and the third to uremia. Of the two deaths in the diffuse group, one was due to erysipelas, and the cause of the death in the other was unknown.

In four, or 10 per cent, of the thirty-eight cases of glomerular nephritis, the condition became chronic, and in five or 27 per cent, of the eighteen cases of tubular and diffuse nephritis, the condition became chronic.

Persistent infection plays a definite rôle in the production of chronic nephritis. Of the four patients with glomerular nephritis that became chronic, one had three attacks of erysipelas and chronic otitis which later led to repeated mastoid operations. Another patient had chronic otitis with mastoiditis; one patient had a chronic renal infection on an obstructive basis, and in the last patient the condition followed scarlet fever. In two of the cases of tubular nephritis the condition became chronic; one patient had chronic infection of the upper respiratory tract with frequent attacks of bronchitis and died of pneumococcus peritonitis, and in the other it was impossible to demonstrate any focus of infection. The tendency of this condition to become chronic, irrespective of demonstrable infection, is well known. Of the three acute diffuse cases in which the condition became chronic, one patient had a chronic sinus infection with repeated attacks of bronchopneumonia, another had a chronic pharyngeal infection with an occasional acute sinus infection, and in the other it was not possible to demonstrate any focus of infection.

The occurrence of uremia has an effect on the immediate prognosis, the cases in which it was present giving a mortality of 23 per cent, as compared to a total mortality of 9 per cent. It has no effect on the chronicity, the patients surviving an attack of uremia having no greater tendency to develop chronic nephritis.

As shown in table 5 (not presented here), there is a higher proportion of deaths and chronicity in those cases showing nitrogen retention than in those not showing nitrogen retention.

A larger percentage of patients who did not have gross hematuria showed a clear urine on discharge than did those who had a gross hematuria. In no patient without hematuria did the condition go on to chronicity. Both of the patients in the glomerular group whose death was due to uremia had gross hematuria.

From a study of the occurrence of edema and hypertension in this series, it was not possible to conclude that there was any relation between the presence of these factors and the mortality or the tendency to chronicity.

Summary.—1. The prognosis in glomerular nephritis—the type of nephritis that is characterized by hematuria, hypertension and nitrogen retention—is better than it is in the tubular and diffuse forms of nephritis in which edema and albuminuria are the features. The mortality in glomerular nephritis is 5.4 per cent, as compared to a total mortality of 9 and 27 per cent in tubular and diffuse nephritis. In only 10 per cent of the cases of glomerular nephritis did the condition become chronic as compared to 27 per cent of the cases of tubular and diffuse nephritis.

2. The relation of infection to the production of acute nephritis is clearly shown. Persistent infection in our series of cases was definitely related to the production of chronic nephritis.

DISCUSSION

DR. CHARLES A. ALDRICH, Winnetka, Ill.: I have been engaged in a similar sort of survey for about the same time as Dr. Lyttle, but I have had a slightly different method of approach. I feel that I was not dealing with the various aspects of the same disease so that I could classify different types of nephritis, but that I was seeing several different diseases that affected the kidney as well as other organs in the body.

As I look over my cases, I wonder whether one has a right to say that chronic glomerular nephritis is a result of acute hemorrhagic nephritis. I have 24 cases which I call chronic glomerular nephritis and about 125 cases of what I call acute hemorrhagic nephritis, and it is not conclusively shown that in any instance the chronic resulted from the acute.

According to the histories, the vast majority of cases of glomerular nephritis show no acute onset. One cannot usually date the development from an acute streptococcic condition of the throat or from pneumonia, as in the cases of acute hemorrhagic nephritis. The patients began to show swelling or to pass blood in

the urine without other symptoms, and I wonder whether this is not a primarily different pathologic process from that in the ordinary case of acute hemorrhagic nephritis.

In our experience, we have found cases of nephrosis in which there were tubular changes but no glomerular changes. Contrary to what is generally stated in the literature, these cases may show a moderate degree of hypertension, as high as 120 in children 4 or 5 years old but not the blood pressure of 180 found in patients with glomerular nephritis.

I think that the only way to differentiate between the two groups with hemorrhagic urine is by the clinical course, and I do not pretend to be able to make a diagnosis when I first see the patient. So many times I have seen patients whom I thought had chronic glomerular nephritis and in whom the condition cleared up that I always consider my original diagnosis provisional. One has to wait and watch the course of the disease before one can tell what is its nature.

One other point that I have noticed in these cases is that practically all of the cases of chronic glomerular nephritis show severe edema at some time or other. The edema subsides, and there is little likelihood of its recurrence if the patients are under a careful regimen. In my opinion, these cases should not be confused with nephrosis.

I agree with what Dr. Lyttle said about the cure of the tubular type of nephritis. I have had about five patients who have gotten well. I do not think that anything I did caused the cure in any case. It is interesting to note that all five patients were cured following temperatures running as high as 105. I have made some effort to produce fever and thus obtain cures but have been unable to do so as yet.

DISCUSSION

DR. KENNETH D. BLACKFAN: I should like to ask Dr. Lyttle whether he has observed changes in the thyroid gland at autopsy. I have recently seen three instances with extensive degenerative changes in this organ.

DR. D. M. COWIE: The classification of nephritis in children is difficult and confusing. In the acute or chronic glomerular nephritis such as has been described one almost invariably finds changes in the blood pressure. In the Vollard and Fahr focal nephritis in which hematuria is a characteristic observation, another classic symptom is said to be increase in the blood pressure. In the case I described in my paper on "Metabolic Studies on Nephrosis," there was no increase in the blood pressure during the nephritic stage nor during subsequent stages.

With regard to cholesterol, Maxwell described a number of cases of acute glomerular nephritis showing a high blood cholesterol content. The cholesterol value, however, does not go so high in the acute forms as in the chronic forms of nephritis with edema.

In regard to the lipoid changes that often take place, the pathologic report in cases of so-called nephrosis records a variable degree of lipoid degeneration of the tubules. Lipoid or double refracting bodies are also found in the interstitial tissues of the kidney. Lipoid changes in other tissues of the body also occur in these cases. It seems to me that in the group in which our case belongs we are dealing with changes in the body that are not necessarily confined to the kidney but take place in other organisms as well. Dr. Blackfan spoke of the thyroid being involved. This fits in well with the conception of nephrosis as a general disease.

It seems to me that much information is going to come from a more intricate study of the changes taking place in the membranes of the body and of the way in which certain etiologic factors affect the cell membrane. Some interesting work has been done in Chicago by Dr. Louis Leiter who produced edema by bleeding dogs and putting back into the blood only a corresponding amount of the formed elements of the blood. When he bled the animals and did not put the blood cells back, the edema did not appear. This lends support to the idea that the edema is due to a lowering of the serum protein to a certain point and fits in nicely with the observations I have made on nephrosis.

With regard to nitrogen retention, in 1916, Dr. Mosenthal showed that the retention of nitrogen does not necessarily mean damage to the kidney. In order to tell whether the kidney is responsible for holding the nitrogen back, a goodly series of determinations of nonprotein nitrogen in the blood must be carried on with the metabolism studies. Some authors arguing against high protein feeding in nephritis or allied disorders base their claims on the premise that during the high protein intake there is a marked positive nitrogen balance. In the absence of a high nonprotein nitrogen in these cases, it is probable that the nitrogen is being retained in normal nitrogen storehouses.

DISCUSSION

DR. JOHN LYTTLE: In one case in which the thyroid was examined, it was not possible to find any evidence of degeneration in this gland, and in the other the autopsy was incomplete. But three cases of tubular nephritis were definitely, clinically at any rate, of subthyroid etiology.

I have treated most of those patients at one time or another with large doses of thyroid, such as Ebstein suggested. The results were variable. It was sometimes possible to control the edema and albuminuria but never with any regularity.

SPLENIC PUNCTURE AS A DIAGNOSTIC PROCEDURE IN INFANCY AND CHILDHOOD. DR. JULIUS H. HESS.

From a pathologic consideration the increase in size of the spleen may be due either to the hyperplasia of its normal structural elements, the storage of abnormal substances or the development of a new tissue which may be inflammatory or neoplastic in nature.

By means of splenic puncture, qualitative changes in the cell structure of the splenic pulp are readily recognized. The interpretation of quantitative changes in both normal and abnormal cells is less definite. Comparative studies of the cellular elements in the circulating blood and the splenic material will aid in clarifying the activity of the spleen in some of the blood dyscrasias.

Cells obtained through splenic puncture can best be evaluated through a conception of, first, cells derived from the normal splenic substance and, second, elements brought to the spleen by the circulating blood.

Technic.—In the presence of a large spleen, puncture can be performed without difficulty. With the patient in a recumbent position, the spleen is held firmly against the abdominal wall with the left hand. For children, a needle about 3 cm. long, attached to a well ground 2 or 5 cc. glass syringe is used. I have found a 22 gage needle with a blunt bevel most satisfactory, as with a fine needle there is less danger of injury. In young children at least a partial anesthesia is recommended, because of the danger of rupturing the spleen during struggling. Only moderate suction should be used. The plunger should not be released until the needle is withdrawn; otherwise, the splenic content will be lost through return of the piston by the negative pressure created. Under no circumstances should more than a few drops be withdrawn.

Following puncture, from 0.2 to 0.3 cc. of 1:1,000 epinephrine solution should be injected subcutaneously. This has a direct action on the capsule of the spleen, causing contraction. In the presence of prolonged bleeding or coagulation time, splenic puncture should not be done.

Classification of Splenomegalies in Childhood from the Standpoint of Value of Splenic Puncture.—I. Splenomegaly associated with dysfunction of hematopoietic system.

a. Anemias secondary to defective mineral metabolism.
b. Anemias secondary to defective regeneration.
c. Anemias secondary to increased blood destruction.
d. Purpura hemorrhagica.
e. Leukemias.

II. Splenomegaly associated with storage disorders of the reticulo-endothelial system.

a. Diabetic lipemia.

b. Niemann-Pick's disease.

c. Gaucher's disease.

III. Splenomegaly secondary to bacterial and spirochetal infections.

IV. Protozoal and parasitic splenomegalies.

a. Malaria.

b. Tropical diseases.

V. Tumors of the spleen.

Summary.—It may be stated that splenic puncture may be of value in substantiating the diagnosis of anemias secondary to defective degeneration, such as von Jaksch's syndrome, in subacute and chronic cases of aleukemic types of myelogenous and lymphatic leukemias, Niemann-Pick's disease, Gaucher's disease and exceptional cases of bacterial and protozoal splenomegalies. It may be of prognostic value preceding splenectomy in exceptional cases of hemorrhagic purpura.

Splenic puncture is contraindicated in the symptomatic purpuras, hemophilia, acute bacterial infections and in tumors of the spleen due to hemangiomas, cysts and malignant tumors.

DISCUSSION

DR. ISAAC A. ABT: What I have to say is not exactly apropos. Last fall and winter, while abroad I saw Prof. William Knopfelnacher take the bone marrow to diagnose Gaucher's disease, aplastic anemia and Niemann-Pick's disease. From the diagnostic standpoint, the results were excellent.

He secured a small amount of marrow, had it hardened and stained by his pathologist, and in every instance was able to verify a suspected clinical diagnosis or in other instances to exclude certain suppositions.

I merely mention this as another method that may be employed in the diagnosis of these diseases of the blood.

DR. KENNETH D. BLACKFAN: I think Dr. Hess' conclusion that splenic puncture may be of value is quite true. However, in this country physicians have hesitated to use it so freely, as it is a procedure not without danger.

In regard to Niemann-Pick's disease and Gaucher's disease, there is good reason to suppose that there are other evidences supporting the diagnosis, without always resorting to splenic puncture. In one case of Niemann-Pick's disease, I found vacuolization of the leukocytes, particularly of the mononuclear forms. In Gaucher's disease, I have seen xanthomatous patches on the inner side of the cornea. Such manifestations taken with the other clinical observations should be regarded as most suggestive of these conditions.

DR. D. M. COWIE: I want to say a word in favor of splenic puncture. I am wondering what size needle Dr. Hess uses. For many years I did splenic puncture in all cases of enlarged spleen without reference to what the condition was. I used a no. 22 ordinarily long hypodermic needle attached to a small syringe, usually a 1 cc. tuberculin Luer syringe. I believe that this procedure will cause no more damage than an ordinary hypodermic injection will in any of the hemorrhagic diseases.

With the new impetus that has been given to hematology by the work of Sabine, Peabody and others, it seems to me that quite a great deal of information may be obtained by systematic study of fluid obtained by splenic puncture. As Dr. Hess has described it, "the spleen is pushed forward to the abdominal wall," the needle is inserted, and the plunger is pulled out and held for about a minute. The fluid may come slowly into the syringe, and probably not more than a needleful will be obtained. This is sufficient for a smear. I had one rather serious accident. The child jumped and the needle broke. It could not be extracted, and the abdomen

had to be opened to overcome the painful scratching of the peritoneum that occurred on ordinary or deep inspiration.

POLYSEROSITIS. DR. LOUIS C. SCHROEDER.

The simultaneous or rapidly successive exudation of fluid into the large serous sacs of the body has been known for many years. The case history of a girl, aged 7½ years, is cited to present certain factors which are present in many of the cases.

For two and one-half months there had been no symptoms except edema of the eyelids, which had been diagnosed as angioneurotic edema. Within a period of four days generalized edema and effusions into the pleural sacs, the peritoneum and the pericardium occurred.

After three months there was a general subsidence of all the effusions with marked improvement, but tachycardia and moderate enlargement of the liver persisted. No single outstanding etiologic factor could be definitely determined.

De Leon divided polyserositis into two groups, acute and chronic. The former is further subdivided into primary and secondary. In the primary group the condition may be due to tuberculosis, rheumatism, syphilis, new growths or leukemia. In the secondary group, it is the result of cardiac, renal or hepatic disease. The chronic group may follow in the wake of the acute forms and is responsible for the many combinations to which the names of various investigators have been applied, such as Pick, Hutinel and Fernet.

Aside from those cases occurring in the course of a rapid acute infection with bacteremia, tuberculosis is probably responsible for the majority of cases. Rheumatism, syphilis and new growths are the next most common causes.

Comby divides polyserositis into four time periods: (1) the exudative, with formation of fluid in the pleural, pericardial and peritoneal sacs; (2) the absorption stage, with sclerotic changes; (3) a latent stage, with incomplete absorption but with distinct compensation and, (4) a terminal stage after a longer or shorter period leading to death.

The case presented showed an abnormal distribution of the albumin-globulin fraction of the blood plasma, a factor noted by Rust in a case of generalized edema of unknown cause.

In polyserositis of childhood, if the symptoms point to the liver or the peritoneum as being the first involved, tuberculosis is most certainly the likely cause. If the symptoms and signs are those of cardiac failure, pericarditis, probably rheumatic or tuberculous, will probably be found.

Fourth Session, May 21, 2:00 p. m.

THE ANAPHYLACTIC SENSITIZATION OF GUINEA-PIGS TO SCARLATINAL STREPTOCOCCUS FILTRATE. DR. JEAN V. COOKE.

Cultures and filtrates of streptococci of scarlatinal origin were used in a series of experiments in sensitizing guinea-pigs, and the animals were tested four or more weeks later by the Schultz-Dale technic for hypersensitivity. Varying intervals between injections and different quantities of filtrate were used in the sensitizing injections. The best results were obtained by giving daily subcutaneous injections of small amounts of filtrate for from six to ten days and testing the animals four or five weeks later. A certain number of such animals gave typical anaphylactic reactions.

Although guinea-pigs were not regularly sensitized to scarlatinal streptococcus filtrate following the methods used, a sufficient number gave typical Schultz-Dale reactions to warrant the conclusion that such filtrates contain anaphylactogenic substances. It seems probable that these substances are derived from the streptococcus, and it is possible that they are identical with the so-called scarlatinal streptococcus toxin.

INFECTIOUS MONONUCLEOSIS WITH LEUKOPENIA. DR. T. C. HEMPELMANN.

Throat infections often produce profound alterations in the differential white blood count, as, for example, that seen in agranulocytic angina and in infectious mononucleosis. In addition to these, during the past year in St. Louis, a small number of children was observed who presented a new clinical picture, namely, fever, evidence of nonmembranous infection of the throat, some degree of adenopathy especially involving the cervical glands, and a striking leukopenia with relative and absolute reduction in the polymorphonuclear neutrophils and a corresponding increase in the mononuclear cells. The temperature ranged from 99.5 to 104 F. and had subsided within one or two weeks. Following the initial respiratory infection, the temperature may rise again coincidently with the glandular involvement. The latter was often pronounced, but in some instances only slight enlargement could be made out. The spleen may or may not be enlarged. Although these children did not appear to be very sick and were often up and around, all showed a marked leukopenia, values as low as 2,450 cells per cubic millimeter being observed, and the differential count showing only 3 per cent polymorphonuclear neutrophils and 94 per cent mononuclear cells, 87 per cent of which were classed as small lymphocytes. Rapid recovery was the rule, and all children have remained well since the attack.

In all the case histories of infectious mononucleosis at the St. Louis Children's Hospital, as well as in 570 records of acute lymphadenitis and tonsillitis, no similar clinical and hematologic pictures were found. Two typical case histories with leukocyte counts are appended.

DISCUSSION

DR. HENRY J. GERSTENBERGER: I should like to know what the platelet counts were.

DR. T. C. HEMPELMANN: No platelet counts were made, but there was no tendency to bleed in any of the patients.

IMPROVED METHOD FOR THE RESTORATION OF BODY FLUIDS. DR. ALEXIS F. HARTMANN.

Dehydration of body tissues and chemical changes such as acidosis or alkalosis occur frequently in sick infants and children and are often serious enough in themselves to cause death. At present parenteral administration of physiologic solution of sodium chloride or Ringer's solution, together with dextrose, is a widely used method of treatment for such conditions, irrespective of the type of chemical disorder. With the aid of more recent chemical studies made possible by development of accurate micromethods of blood and urine analysis, the limitations of such treatment have been recognized and it has been found possible, for example, to relieve much more satisfactorily the acidosis associated with severe diarrhea by the additional use of alkali in proper dosage.

Lantern slides were shown demonstrating chemical changes due to loss of gastric and intestinal secretions alone and combined and to renal insufficiency.

From such studies it can be noted that the more serious disturbances involve loss in some combination of water, the chlorine ion and base ion and that by proper administration of Ringer's solution, dextrose and sodium bicarbonate, prompt restoration of altered body fluids can usually be accomplished.

With the hope, however, of rendering unnecessary special chemical examination either for diagnosis or therapeutic checkup, the authors have developed a new combined solution of the following composition: sodium chloride, 95 mg. B+; potassium chloride, 5 mg. B+; calcium chloride, 2.5 mg. B+; sodium lactate, 25 mg. B+.

This solution supplies adequately, if needed (but without danger, if not), water, the chlorine ion, alkali (by oxidation of the sodium lactate), potassium for the cell, and dextrose and may be administered subcutaneously, intraperitoneally or intravenously.

DISCUSSION

DR. JAMES L. GAMBLE: If dehydration is accompanied by alkalosis, I should expect that the solution which Dr. Hartmann suggests using would cause further increase of plasma bicarbonate for the reason that in the presence of the base deficit due to dehydration base given as bicarbonate would not be removed in the urine.

DR. ALEXIS F. HARTMANN: Dr. Gamble's point, that sodium lactate administered in the presence of alkalosis associated with diminution of total fixed base might be expected to increase the alkalosis, deserves special comment. At first it was felt that it would be necessary to use two solutions: Ringer's solution for changes associated with low chloride and base, and sodium lactate for patients with acidosis. It was found, however, that the combined solution worked equally as well in animals with either type of change.

It is possible that dogs with alkalosis excrete more unchanged sodium lactate than dogs with acidosis. I have not as yet followed the excretion of lactate in the urine. I intend shortly to do this, as well as to follow at short intervals the changes in the blood and urine brought about by the administration of the combined solution.

RHEUMATISM. DR. EDITH I. M. IRVINE-JONES.

The bacteriologic study of the streptococci of the upper respiratory tract in rheumatic subjects shows no difference in morphology or immunologic reactions from those obtained from the throats of normal subjects. Injections of dilute filtrates of those organisms from either series show a much higher percentage of positive reactions in rheumatic subjects than in the nonrheumatic controls. It was found that the degree of skin sensitivity to filtrates of streptococci varied with the degree of rheumatic infection, that the highest percentage of positive reacions occurred in acute rheumatic fever, the lowest percentage in acute carditis. It was found further that after convalescence became established in acute rheumatic fever and chorea the skin tests tended to become negative, while as recovery in acute carditis occurred the tests tended to become positive. The evidence points to rheumatic fever being an allergic response to the common streptococci of the upper respiratory tract. The percentage of rheumatic subjects reacting positively to the Dick test is lower than that of nonrheumatic children. Rheumatic children with negative Dick tests show a higher percentage of positive skin tests to intradermal streptococcus filtrates than do those with a positive Dick test.

It is felt that the high percentage of negative Dick reactions in rheumatic children is probably further evidence of their tendency to infections of the upper respiratory tract.

A clinical correlation of these bacteriologic observations was made in 45 families in which more than one case of rheumatism or chorea occurred in the same family. This included 131 rheumatic patients (84 children) and 138 nonrheumatic patients. It was thought that if the multiple cases depended on the influence of heredity, as has been shown in atopic hypersensitiveness, the proportion of children affected would be proportional to the parental involvement. No difference was found in the number of children affected in any family irrespective of the numbers of parents who had suffered from the disease. It was also found that the age of onset was not lower in those families in which both parents were affected than in those in which only one parent was rheumatic. The coloring of rheumatic children did not differ from that of the nonrheumatic children of the same family, but there was a larger percentage of blond and redhaired children in rheumatic families than in the population at large. A study of the blood groups similar to that made by Hirzfeld and Brokman in diphtheria and by Levine in atopic hypersensitiveness did not show any correlation between the blood groups of the affected persons and the tendency to rheumatic infection.

Evidence for the contagious nature of rheumatism is considerable. In twenty-seven instances two cases of rheumatic fever occurred simultaneously; in five

instances, three cases; in one instance, four cases, a total of seventy-three attacks. Seventy-two further attacks of rheumatic fever occurred in the group at intervals. Instances exist in which unrelated children develop rheumatic fever when the influence of heredity can be ruled out. The incidence of rheumatism among the children in a family was higher than the incidence of rheumatism between parent and child. Children who slept together and who were of approximately the same age were more liable to simultaneous attacks than children who were less in contact with each other.

During the last two years we have watched all the members in rheumatic families and have been able to show that when one attack of acute rheumatic fever occurs frequently other members of the family suffer from sore throat and bronchitis, thus pointing to a common infection. This fact may be correlated with the finding of similar organisms in the throats of rheumatic and nonrheumatic subjects associated with the difference in the skin reactions in those subjects showing the rheumatic syndrome. While rheumatic fever thus appears to be communicable, the influence of a hereditary predisposition is as yet undetermined.

Eczema. Dr. Francis Scott Smyth.

It has been demonstrated that the blood of some infants with eczema contains a toxic fraction which is, however, variable in titer. This substance appears to be unrelated to the "reagen" of Coca and to any toxic product so far observed for human serum except that demonstrated in urticaria due to cold. It may be similar to the hypothetic "histamine-like" substance produced by trauma and described by Lewis, but the latter substance was not present in sufficient titer for passive transfer. The presence of this substance may explain the marked seasonal variation of eczema with preference for winter, the extensive involvement of exposed areas of skin, the obvious effect of trauma and the reported beneficial effect of graded therapy (e. g., light) which increases tolerance for the physical agents. The observations also support the view that in infantile eczema, sensitivity to physical agents plays an important part and that similar to the sensitivity of foodstuffs, there may be a parallel response in the blood as evidence of a general condition, not merely a skin disease.

The Relationship Between Colic and Eczema in Early Infancy. Dr. Park J. White.

Summary and Conclusions.—1. Very young infants with "true colic," or vagogenic gastro-enterospasm who later develop eczema are found almost three times as commonly as those suffering from either condition alone.

2. An allergic family history is about equally frequent (30 or 40 per cent) for infants with eczema, with colic, or with both.

3. The usual sequence is: (*a*) colic, (*b*) diarrhea, (*c*) vomiting—all at from 2 to 4 weeks of age, and (*d*) eczema, at about 10 weeks of age.

4. Atropine is effective almost three times as frequently in infants with colic alone as it is in infants with both colic and eczema.

5. Thick cereal feeding may be successful in infants with colic who have not improved after the administration of atropine.

6. There is no evidence that thick cereal feeding predisposes to eczema.

7. Possibly because of hyperacidity associated with hypermotility, gastro-enterospastic infants tolerate sweet milk better than they do lactic acid milk.

8. "The exudative diathesis," "vagotonia," and "vagogenic gastro-enterospasm," with or without eczema, probably have a common allergic basis.

Renal Rickets. Dr. L. Schoenthal.

Since renal rickets or renal dwarfism or infantilism was first recognized as a clinical entity by British authors, several cases have been described in this country.

Hunt reviewed the cases reported in the literature (1927). I thought it worth while to report this case because the patient was followed over a long period of time and the metabolism was studied closely.

A boy, aged 8 years, who weighed 7 pounds and 3 ounces (3,260.19 Gm.) at birth, in 1921, had always been underweight and under height; he walked at the age of 16 months. The present weight was 37¾ pounds (17.1 Kg.), 16¾ pounds (7.6 Kg.) less than normal; the height, 39¾ inches (100.3 cm.), 8⁹⁄₁₀ inches (22.5 cm.) less than normal. He had always been pale; the highest red blood cell count in three years was 2,600,000, in spite of frequent transfusions. In 1924, when the boy was 3 years old, rickets was diagnosed clinically. Ordinary treatment for rickets failed to cause improvement. In 1926, he was admitted to the orthopedic clinic for operation for genu valgum. The diagnosis of rickets was confirmed roentgenologically (acute form). A trace of albumin was found in the urine, and he was sent to the St. Louis Children's Hospital. He has been under observation since that time. In 1926 the blood and urine showed typical changes of chronic renal insufficiency; the blood showed: low carbon dioxide, low chloride, low total base and calcium, high phosphate; nonprotein nitrogen, over 200 mg. Infections accompanied by vomiting, dehydration and convulsions produced an increase in acidosis. At one time osmolar concentration of the serum rose to 380 osmolar mm. The administration of Ringer's solution, dextrose and bicarbonate together with frequent blood transfusions restored the acid-base equilibrium to the status antecoincident with clinical improvement. A remarkable parallelism between nonprotein nitrogen and phosphorus was noted, while the calcium showed changes in the opposite direction. The urine was always pale, of a fixed low specific gravity and nearly neutral reaction. The phenolsulphonphthalein excretion was between 5 and 10 per cent. A little ammonia was present in the urine. The patient was therefore put on a diet containing alkaline ash. For two years he did well on this diet. In November, 1928, he was put on a diet of determined acid-base content. The total stool and urine output was analyzed. For the first three days, with a low food intake, he showed a positive base and calcium balance, while the phosphorus and nitrogen balance was negative. Sodium bicarbonate was then added to the diet, in an amount calculated to be sufficient to restore bicarbonate concentration of body fluids. Following a further reduction of food intake, he had a completely negative balance, as the base excreted in the stool and urine remained unchanged. Calcium was chiefly lost through the stool, as excretion in the urine was extremely small. For the whole period, however, the base balance remained positive.

Other salts, disodium phosphate, calcium acetate and calcium lactate, were added to the diet; disodium phosphate, as sodium bicarbonate, produced an increase of phosphorus in the blood after oral administration with a lowering of calcium; calcium acetate and calcium lactate decreased the phosphorus to lower values but did not lead to an increase in the calcium concentration. The blood calcium x phosphate (Howland, Kramer) was always higher than 50 and above the rachitic zone. The ionic product $(Ca^{++}) \times (P^{---})$ (Holt) showed either normal values or those of healing rickets. It is curious to observe that both products indicated active rickets after the administration of calcium acetate. The last roentgenograms show evidence of healing rickets. This boy has had infantile rickets. Because of renal insufficiency with acidosis and high phosphate, the rachitic changes persisted. An addition of alkali to the diet or parenterally during infection proved to be of benefit to the acid-base metabolism and produced positive base-balance even in the period of low food intake. In view of the definite destruction of kidney tissue in most of these cases, this seems to us the only possible attempt to influence the course of the disease.

DISCUSSION

DR. HENRY J. GERSTENBERGER: What were the calcium and inorganic phosphate levels in the blood serum?

DR. L. SCHOENTHAL: The calcium level was always below normal, varying between 5.3 and 8.8 mg. per hundred cubic centimeters. The phosphorus was always increased and showed values between 6.5 and 17.2 mg. per hundred cubic centimeters.

DR. BELÁ SCHICK: In my department I also observed a case of renal rickets. The child, now 7 years of age, surely had symptoms of renal insufficiency in early childhood. He was always pale and delicate, drank a great deal of water, was always thirsty, and showed enuresis. Symptoms of bone deformities became marked at the age of 5½ years after an attack of measles. Pain in the legs, a toddling gait and bone deformity caused this child to pay frequent visits to an orthopedic hospital. Laboratory tests showed: low specific gravity of the urine, lack of ability to concentrate, casts high, urea nitrogen in the blood serum (143 mg.), and later, a high cholesterin content (up to 518). The blood calcium was high (from 10.6 to 11); the phosphorus content was high in the beginning (8) and later was lower (4.2). The anemia (35 per cent hemoglobin) persisted and was only temporarily improved by transfusion. Treatment with ergosterol brought about some healing of the process of rickets. The case will be further studied and a report published by Karelitz and Kolomoytzoff.

(Dr. Schick showed pictures of the child and x-ray pictures of the bone taken at different times while the child was under observation.)

DR. BENJAMIN KRAMER: In 1924, I analyzed the serum of a child with renal dwarfism. The calcium and inorganic phosphorus were both in the neighborhood of 5 mg. per hundred cubic centimeters of serum, giving a product of 25. There was a transverse fracture of the lower end of the tibia. This is consistent with the observations of Howland and Kramer in patients with active rickets.

In a recent review of the subject of renal rickets, Parsons reported serum calcium values of from 8 to 16 mg. per hundred cubic centimeters of serum. The inorganic phosphorus was also high. The Ca X P products are all above the rachitic level whether calculated according to Howland and Kramer or Holt. One must be sure that the rachitic process is active at the time the analyses of the blood serum are made. The roentgenogram should be helpful in determining this fact. Recent studies on in vitro calcification have shown that several factors aside from the Ca X P product may influence this process; namely, the concentration of magnesium, the total ionic strength of the serum, and probably certain end-products of protein hydrolysis, such as, amino-acids and urea (Freudenberg and György).

The form in which the calcium exists in serum is important. Calcium forms soluble, unionized compounds with citric acid so that calcification fails to occur even with a high Ca X P product.

DR. L. SCHOENTHAL: I consider the case reported of the low calcium and high phosphorus type of rickets, as shown by Shipley and his co-workers. I did not want to theorize as to the cause of this condition, aside from the chemical facts. Different attempts have been made to explain it on the theory of a disturbance of the glands of internal secretion, but so far there is nothing certain about it.

Rachitic changes were shown by the x-rays.

CHRONIC ADHESIVE PERICARDITIS. DR. HUGH MCCULLOCH and DR. WILLIAM R. WILSON.

Chronic adhesive pericarditis usually follows rheumatic fever and in children may be one of two different types. In one, the child has an acute attack of precordial pain with high fever, prostration, friction rub, usually with some amount of fluid in the pericardial sac and signs of myocardial and valvular injury. These attacks may or may not follow acute tonsillitis. They last from a few days to a few weeks and usually clear up, leaving the child in his previous state.

We have noted at the St. Louis Children's Hospital that when children with fair complexion and reddish blonde hair have rheumatic fever with pericarditis,

the attack corresponds to this description. This form of fibrinous or serofibrinous pericarditis is essentially exudative in nature and belongs in this group described by Swift. The second type of reaction results in chronic adhesive pericarditis. A history of acute attacks of pericarditis in these is lacking. The diagnosis is made either when the child comes for first observation or when after being continuously under observation, there comes a time when a diagnosis can be made with no definite onset to be noted. This type of pericarditis is more frequently seen in the sallow semiblonde type of child who shows other signs of a proliferative lesion, notably rheumatic nodules around the joints. This reaction conforms to the proliferative type described by Swift as hyperergic, in the nature of the response to the infection.

The clinical diagnosis of chronic adhesive pericarditis is often difficult. The signs which suggest such a condition are: (*a*) A history of attacks of precordial pain; (*b*) deformity of the anterior chest wall over the heart; (*c*) congestive heart failure of severe degree; (*d*) signs of adhesions to neighboring structures; (*e*) fluoroscopic confirmation of these adhesions; (*f*) electrocardiograms with fixation of the cardiac axis when the patient is shifted from the left to the right lateral recumbent position, and signs of disturbances of mechanism.

The effect of adhesive pericarditis on the heart is seriously to impede its contraction and to throw additional strain on the heart muscle. In a heart muscle already injured by rheumatic fever, this embarrassment is sufficient to cause congestive heart failure. When the right ventricle becomes adherent to the pericardium and eventually to the anterior chest wall, there is the added strain of contraction against a fixed structure. It is probable that extreme degrees of cardiac failure which resist ordinary medical treatment are accounted for by this right-sided cardiac failure.

To relieve these patients cardiolysis has been proposed to set the heart free from this contraction against a fixed structure. The operation was proposed by Brauer in 1903 and modified by Schmieden and has been performed successfully on human beings. The results have been sufficiently satisfactory to warrant continuing the use of the operation. This operation has been done successfully on two children in the St. Louis Children's Hospital. Under local anesthesia, the anterior chest wall lying directly over the heart has been resected and removed. The relief of congestive heart failure and disturbances in mechanism of the heart in a child, aged 4 years, was immediate and definite. She died about four months later with acute lobar pneumonia, without signs of congestive heart failure. The other child, aged 15, was greatly relieved. He showed fibrillation of the auricles before operation and this condition continued. He was able to be more active and showed no signs of congestive heart failure.

Fifth Session, May 22, 8: 30 a. m.

SCARLET FEVER. DR. GEORGE F. DICK.

This paper will appear in full in a later issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN.

DISCUSSION

DR. L. R. DE BUYS: How long after the last immunizing dose is immunity established in regard to scarlet fever? Is there any objection to giving the immunizing dose of scarlet fever toxin together with the toxin-antitoxin of diphtheria? I know that Zingher was doing that for some time before his death. To what does Dr. Dick ascribe the rather severe reaction which follows the administration of the antiscarlatinal serum which occurs four or five days after its administration? I mean the inability of the patient to move and the extreme pains in the joints, etc. This does not occur after the administration of the antidiphtheria serum, so that it probably is not a serum reaction per se.

DR. GEORGE F. DICK: In regard to Dr. De Buy's question, How long after the fifth immunizing dose is immunity established in regard to scarlet fever? The immunity begins to develop soon after prophylactic injections of scarlet fever toxin, so that two weeks after the last dose a skin test can be made.

In regard to the reaction after the administration of scarlet fever serum, I do not find any particular difference between diphtheria and scarlet fever antitoxin, as far as serum reactions are concerned. It depends largely on the preparation of antitoxin that is used. Antitoxin varies a great deal; any serum, as a matter of fact, varies a great deal in the production of serum disease due to differences in the method of concentration.

One manufacturer has been having as much as from 50 to 60 per cent of serum reaction with the concentration method used with both diphtheria and scarlet fever antitoxins, because they are concentrated in the same way.

At this time, I am told, an experiment is being made at the University of Illinois to find out what is the matter with that method of concentration. As everyone knows, the fresh serum gives more serum reactions than the serum that is allowed to stand, but the method of concentration is the most important thing, and on that will depend the amount of serum reactions that obtain, and it will be the same approximately for any serum, tetanus, scarlet fever, or others. It depends to a less degree on the quantity of serum used.

At times, there has been at Durand Hospital more serum disease caused by scarlet fever serum than by diphtheria serum, but recently there have been more reactions from diphtheria antitoxin than from that of scarlet fever. We have been particular about the tests for the proper refinements of serum, and the manufacturers who are cooperating with us, therefore, produce serums giving a minimum of serum disease.

As to the question regarding giving the immunizing dose of scarlet fever antitoxin with the antitoxin of diphtheria, we do not advise that.

Reactions occur with the scarlet fever toxin and also with the diphtheria toxin-antitoxin, and I think that if one gives them both together it is reasonable to suppose that in some cases one may get more reaction. But aside from that, there is no objection.

SERUMS AND VACCINES IN THE PREVENTION AND TREATMENT OF DISEASE. DR. BENJAMIN WHITE.

Because of the rapid progress of biologic therapy, it is advisable at times to make a critical appraisal of the many serums and vaccines that are offered to the medical profession. Such an appraisal should be based on the scientific knowledge of the chemical composition of such products, their physiologic action in the human body, and the immunizing response which they call forth.

From these criteria, it is possible to predict with a fair degree of accuracy what one may expect from any given serum and vaccine. Clinical evidence is valuable only when it represents controlled observations.

Among the various products discussed were the antivirus of Besredka, which has found favor in Europe but has not been accepted here. The relative merits of diphtheria toxin-antitoxin and toxoids were discussed, and while toxoid or anatoxin is a better immunizing agent, the toxin-antitoxin mixture gives none of the reactions which the latter produces in children over 6 years of age. The former is still the preferred agent. The danger of sensitization by the usual toxin-antitoxin mixtures was not felt to be great.

Whooping cough vaccine was discussed and the opinion given that there was no proof that this vaccine would prevent whooping cough or greatly modify an attack.

The various preparations of rabies vaccine were mentioned, and it was recommended that the full twenty-one-day treatment be given to all persons bitten by rabid animals.

The care necessary in handling vaccine virus and the "multiple pressure method" of vaccination were described, and the necessity of observing immune reactions to vaccine virus was pointed out.

There was a short résumé of the immunologic principles underlying the use of B.C.G. One would expect only a low degree of immunity to be produced, and until it can be definitely proved that this preparation is entirely harmless it would be better to restrict investigations to experimental animals.

Mention was made of the enterovaccines of Besredka, which have not been generally accepted in this country.

The rationale for the use of convalescent serum in anterior poliomyelitis was outlined, and from it one should expect that a potent serum should be of benefit in the early stages of the disease. That such is the case is apparently shown by Aycock's analysis of cases in Massachusetts. The value of isolating meningococci from the spinal fluid in all cases of cerebrospinal meningitis was emphasized. In the event that the particular lot of serum fails to be effective, the organism should then be tested against other lots of serum and a more potent preparation selected.

The proper methods for administering diphtheria antitoxin and the theoretically desirable doses were discussed.

A plea was made to the physicians present that because they were teachers or representatives in their various localities they should apply these various criteria to all biologic products before they recommend their use. Serums and vaccines are products of inestimable value to the medical profession and to public health workers, but the adoption of new preparations should be made only after long and carefully controlled clinical trials, and the physician should not expect more from any of these products than the immunologists claim for them.

DR. HUGH MCCULLOCH, St. Louis: I should like to ask Dr. White if he would say a few words about encephalitis following vaccination for smallpox, as he probably may have had an opportunity to discuss this condition on his trip through Europe.

DR. ARMAND-DELILLE: May I add a few remarks from my own experience in connection with the interesting paper of Dr. White?

Concerning cholera, I have had no experience with the d'Herelle method, but during the World War I observed an interesting demonstration of the efficiency of cholera vaccination (heated vibrio culture). All the soldiers and officers were vaccinated during a severe epidemic of cholera which had developed at Koritza, Albania, a city of about 10,000 inhabitants. During the epidemic, there were about ten deaths a day. The entire civilian population was vaccinated in two weeks, and the epidemic was stopped within that time. None of the French troops developed the disease. My friend Dr. Cantaczcie had a similar experience in the Roumanian army.

As to vaccination against diphtheria, I use Ramon's anatoxin for all children in the hospital except those with acute infections, and with its use I have had no cross-infections with diphtheria. I have not seen reactions in children after the use of this material, although they are seen in adults (nurses and others) with positive Schick tests, the vaccination sometimes producing fever and weakness for a few days following the injection.

Concerning the use of pertussis vaccine, I agree that the Bordet vaccine has no definite beneficial effect. Occasionally, it seems to diminish the severity of the cough, but it has been the experience of every pediatrician that with the employment of about 300 various methods of treatment for pertussis, one or another method may seem beneficial.

In regard to B.C.G. vaccine, I have seen some convincing demonstrations of its efficiency among infants vaccinated with this material. These infants were in contact with tuberculous parents and did not develop any symptoms of tuberculosis. I recently visited my friend, Professor Saye in Barcelona, who had made an important investigation with the use of B.C.G. The housing conditions in Barcelona are poor, and the vaccinated children, therefore, remain in close contact with their tuberculous parents. Some of the children develop mild symptoms of glandular tuberculosis but never die.

My associates and I believe that the Besredka method of immunization by mouth against typhoid and paratyphoid A and B is not perfectly efficient. We prefer to

use the parenteral method (subcutaneous injections). We often use the lipovaccine, that is, bacilli in oil emulsion. We give only one injection, and if no reaction ensues, this may be said to be due to a slow absorption. In France typhoid is no longer observed in the adult male, since he is vaccinated in the army. It is observed only in women and children who have not been vaccinated against typhoid. I, myself, always advise vaccination for children over 7 years of age.

Concerning the dosage of diphtheria antitoxin, a peculiar phenomenon has been observed in Paris. It is necessary to give large doses of antitoxin, which is contrary to the experience of physicians in the country districts, where diphtheria is successfully treated with small doses of serum. I believe that this difference in the required dosage of antitoxin may be due to the fact that an unusual strain of the diphtheria bacillus has developed which is of greater virulence and has a high degree of antitoxin resistance.

DR. BENJAMIN WHITE: I am glad that Dr. Delille has mentioned the severe type of diphtheria prevailing in France. A similar situation exists in other European countries in which many cases of fulminating diphtheria have occurred in the past two years. We have obtained cultures of diphtheria bacilli isolated from these cases and find that the toxin they produce is neutralized by our diphtheria antitoxin. It would seem, then, that physicians should be on the watch for cases of this type and should administer large doses of antitoxin at the earliest possible moment.

The question of hypersensitiveness to horse serum is extremely complex. Following the test intradermic injection of serum, one sees every variety of reaction from the immediate to one appearing twenty-four hours later, and I confess that I do not know the significance of these various reactions. However, if there is no reaction to an intradermic test of horse serum after the lapse of one-half hour, one can safely administer any horse serum product without fear of immediate reaction. When reactions occur, desensitization may be done, but it is not always successful.

DR. BELÁ SCHICK: It was observed during Jenner's time that the smallpox vaccination sould be left without a real dressing. If a dressing is employed the drying up is delayed, and secondary complications are more frequent.

The preference given the Mantoux test over the Pirquet test is apparently due to the fact that active tuberculosis is not as frequent in the United States as it is in Austria or Germany. The tuberculin solution in the original Mantoux test is 1 : 10,000. An injection of 0.1 of this solution gives the same result as the Pirquet test. For diagnostic purposes, a stronger concentration (from 0.1 to 0.2 of 1 : 1,000) is usually recommended. Such solutions may be too strong for children with active tuberculosis, and general reactions are frequently observed, especially in scrofulous children. When the intracutaneous (Mantoux) test is used, the concentration applied should be mentioned. The effect of Calmette's B.C.G. vaccine has not, as yet, been determined sufficiently to allow this method to be employed in general practice. This work still needs careful study, which should be made only under strict control.

DR. JOSEPH BRENNEMANN: If it is a legitimate question, I should like to ask Dr. White what is his opinion of the work of De Cristina and Caronia along these lines.

DR. HENRY F. HELMHOLZ: I should like to ask what procedure Dr. White advocates when a child is likely to be sensitive to horse serum.

DEHYDRATION. DR. J. L. GAMBLE.

In this paper, the author presents a summary of the results of several previously reported experimental studies of dehydration (with S. G. Ross and I. McIver).

The data from these experiments support the following simple explanation of the dehydration which accompanies severe disturbances of gastro-intestinal function: vomiting and diarrhea cause a more or less complete failure of reabsorption of gastro-intestinal secretions, with the consequence that there occurs a progressive withdrawal from the blood plasma of the water and substances used in the con-

struction of these secretions. Data obtained from rabbits with an experimental obstruction at the pylorus demonstrate that the volume of the loss of gastric secretions alone, when reabsorption is thus blocked, is of a magnitude sufficient to explain rapid and extensive dehydration. The premise that loss of water is the result of a loss of substances is used and is supported by the results of analyses of gastric and upper intestinal secretions taken from animals. These data show a total content of substances closely equivalent to that of the blood plasma and also demonstrate that the material lost from the plasma is almost entirely sodium and chloride ion. Physiologic solution of sodium chloride is thus indicated as the primary agent in the treatment of dehydration. The point that water alone will not repair dehydration is stressed by citing an experiment in which isotonic dextrose solution given abundantly to a dog, dehydrated by means of an obstruction at the pylorus, failed to prolong the survival period appreciably. The dextrose is presumed to have been rapidly removed by oxidation. It is well known that in such an experiment salt solution will prolong life for many days.

The analyses of gastro-intestinal secretions provide a probable explanation of the variable change in blood plasma reaction in the presence of dehydration. Gastric secretions contain relatively much more of sodium than of chloride ion, and the reverse is true of duodenal secretions. Vomiting should therefore tend to produce alkalosis and diarrhea, acidosis. The relationship of vomiting and alkalosis is well known. In support of the reverse effect from loss of duodenal secretions, an experiment is cited in which severe acidosis developed in a dog as a result of draining away pancreatic juice by means of an external fistula.

On the basis of tissue analysis, dehydration is regarded as confined to the interstitial fluids and the blood plasma. The unavailability of intracellular water for support of blood plasma volume is explained in terms of differences in the chemical anatomy of the several body fluids; interstitial fluid contains an abundance of sodium and chloride ion, the substances chiefly lost from the plasma, whereas, in intracellular water, these materials are not present in appreciable amounts. Disturbances of physiologic processes and ultimate death are considered sufficiently explained as a result of progressive failure of the function of the blood which ensues when the losses of water and materials from the plasma can no longer be adequately replaced from the interstitial fluid reservoir.

EPILEPSY IN CHILDREN: THE RELATIONSHIP OF WATER BALANCE TO THE OCCURRENCE OF SEIZURES. DR. IRVINE MCQUARRIE.

This paper appears in full in this issue, p. 451.

DISCUSSION ON PAPERS OF DR. GAMBLE AND DR. MC QUARRIE

DR. HENRY F. HELMHOLZ: My associates and I find that in about one third of the cases the diet will free the patient from his attacks, and in an additional 20 or 30 per cent the diet ameliorates the attacks.

We have tried the restriction of fluid in two cases. In a child about 3 years of age, who was having severe convulsive seizures, we were able to control the severe seizures but found that by carrying the restriction of fluid up to a point of hyperthermia the convulsive seizures were replaced by seizures of petit mal. In the other case there was a reduction of the number of attacks without, however, entire freedom from attacks.

DR. IRVINE MCQUARRIE: With reference to the effect of this form of therapy on the occurrence of seizures of petit mal, I would like to cite one of my cases. A girl, aged 8 years, first referred in December, 1928, had been having from fifteen to sixty minor attacks daily for several months. Within a few days after the regimen was begun, the number of seizures was reduced to an average of less than one daily. Two weeks later, they ceased entirely and have not recurred to date, a period of more than four months. While the seizures of petit mal are the last to

disappear, they can usually be controlled in the end, I believe, by persistent use of the special diet and rigid water restriction.

THE CORRELATION OF ULTRAVIOLET ABSORPTION TO THE DEVELOPMENT OF IMMUNITY. DR. FREDERIC W. SCHLUTZ and WILFRED W. WETZEL.

It has been observed that the absorption spectrum for blood serum in the ultraviolet has a characteristic absorption band at 2,800 angstrom units.

Judd Lewis was the first to observe variations from the normal in the absorption curve of various pathologic serums.

In a second publication, Lewis showed that the protein content of serum is the absorbing constituent and gave curves for the absorption of the three protein fractions, pseudoglobulin, euglobulin and albumin.

Stenström and Reinhard showed that a synthesis of the amino-acids in the proportion in which they occur in blood serum gave a similar absorption curve to that of serum.

They attribute the band chiefly to the effect of the tyrosine and tryptophane content of serum.

Studies have already been made of the protein content of pathologic serums and the relation of globulin to albumin.

Wells, and Hurwitz and Meyer found a variation of the globulin-albumin ratio during the course of artificially stimulated immunity.

They found that a temporary decrease of albumin with an increase of globulin took place during the development of immunity.

Other investigators noted similar changes.

The investigations of Lewis, Stenström and others would seem to indicate that the ultraviolet spectroscope has the possibility of becoming a good instrument for determining whether immunity has or has not been acquired against certain infectious diseases.

We propose a study of the absorption spectra of the blood serum in various contagious diseases common to childhood, covering the phases of normality, the incubation period, height of the exanthem, the period of convalescence and the expected return to normal.

By the correlation of data from a large number of cases, we hope to find some constant factor characteristic of the development of immunity.

Our investigations were carried out with a Hilger Type E-3 spectrograph and a Judd Lewis sector-photometer, an underwater tungsten spark being used.

So far, we have collected data on diphtheria immunization and on scarlet fever and measles.

We do not feel that definite conclusions can be drawn from the data so far obtained, but a number of interesting changes have been observed.

A shift in wavelength of the absorption head and foot occurs, which may prove to be of significance.

A somewhat constant increase of total proteins during the period in which immunity presumably develops and the beginnings of a return to the normal after that period have been found.

In some of the cases, there is an indication of increase in the globulin-albumin ratio.

From more spectrographic data, together with quantitative chemical analysis and fractionation of the serums, we can hope to show some consistent change in the proteins during the course of various diseases.

We hope to correlate the spectrographic measurements of total changes in the protein and relative changes in the ratio of the protein fractions with the development of immune reactions in the course of disease.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

April 4, 1929

STAFFORD MCLEAN, M.D., *Presiding*

EXPERIMENTAL PRODUCTION OF ABSCESS OF THE LUNG. DR. E. C. CUTLER.

This article will be published in a later issue of this Journal.

DISCUSSION

DR. H. A. BRAY: In discussing Dr. Cutler's paper, I shall consider only the most important type of pulmonary abscess encountered in man, the one which is characterized by intensely foul sputum.

Dr. Cutler believes that this type of abscess is the result of an embolism, which, subsequent to its lodgment in the lung, is invaded by fusospirochetal organisms, and that they play a secondary rôle in the production of the disease.

Dr. Cutler produced chronic pulmonary abscess experimentally only when he implanted fusospirochetes in the lung through the vascular channels, but he brought forward no experimental proof in support of his view that these organisms are merely secondary invaders, nor did he mention, if I remember correctly, the route of their invasion.

Pathologic studies have demonstrated that pulmonary infarct complicating conditions such as endocarditis rarely become secondarily infected with fusospirochetes. Moreover, these organisms are seldom encountered in the more common diseases of the lung. In 800 specimens of sputum positive for tubercle bacilli which we studied with this point in mind, the fusospirochetal group were found only in five instances, and three of these patients were shown to be suffering from tuberculosis and bronchiectasis. Likewise, in pneumococcus pneumonia these organisms are seldom found.

In the light of these observations, it is open to question whether the spirochetes are merely secondary invaders in the production of pulmonary abscess with foul sputum.

On the other hand, we at Ray Brook, consider it definitely proved that this type of abscess is but one manifestation of the symbiotic activity of a group of anaerobes normally present in the mouth. This so-called fusospirochetal group produces such diverse clinical manifestations as bloody bronchitis, certain types of pneumonia, pulmonary gangrene, empyema, bronchiectasis, pulmonary abscess and combinations of the same. The fusospirochetal group of organisms closely resembles the tubercle bacillus in the chronicity and destructive nature of its lesions and their protean character.

For twenty years we have been interested in these lesions at Ray Brook. My predecessor, Dr. Garvin, outlined the diagnostic standards and introduced the postural treatment for primary bronchiectasis. Much work was done by Avery, White and Lyall to determine the cause of primary bronchiectasis by an exhaustive investigation of the aerobic bacteria in the sputum. Their results were naturally disappointing, for aerobic bacteria are not the cause of the disease.

For the past five years, my associate, Dr. David T. Smith, found fusospirochetal organisms in primary bronchiectasis, pulmonary gangrene, pulmonary abscess and the associated pneumonias so frequently that it suggested to us that they were the primary cause of these pulmonary lesions. More than 100 rabbits, guinea-pigs and mice were inoculated intratracheally with material from these pulmonary lesions. These inoculations resulted in the production of pathologic lesions similar to those found in man. From these pulmonary lesions, Dr. Smith isolated in pure culture the fusiform bacillus, *Treponema microdenteum, Treponema macrodenteum, Vibrio* and anaerobic cocci. He found that no single one of these organisms in pure culture and no combination of two or three of them would reproduce the characteristic

experimental lesions. The presence of all of them was required; i.e., the lesions were the product of a true symbiosis of the entire fusospirochetal group. If the group is considered together as a single causative agent, we might claim fairly that it satisfies the postulates of Koch. It is constantly found in the lesions of the disease; it can be cultivated in pure culture from the lesions; the cultures reproduce the disease in animals, and from the experimental lesions the fusospirochetal group can once more be isolated.

Our studies have convinced us that pulmonary abscess is but one manifestation of a protean pathologic picture due to a fusospirochetal infection.

I shall consider briefly the channels of infection. Dr. Cutler employed the vascular channels to produce pulmonary abscess. It does not follow, however, that this is the only or even the usual route. Gardner, by employing the vascular channels, has produced experimental silicosis of the lung, but clinically the dust is carried to the lung by the respiratory tract. One can readily induce pulmonary tuberculosis in experimental animals by injecting a suspension of tubercle bacilli into a vein, but it is equally easy to do so by placing the bacilli in the trachea.

The buccal cavity is the potential source of fusospirochetal infections of the lung in man, because these organisms are so rarely encountered elsewhere in the body. These anaerobes were present in the mouth in every instance of fusospirochetal infection of the lung observed by us. We have therefore concluded that the buccal cavity is the depot from which the organisms gain access to the lung.

The notable high incidence of pulmonary abscess after tonsillectomy is due to the presence of fusospirochetes in the operative field, and the exceptionally favorable conditions for their aspiration. On bronchoscopic examination Myerson found that the contents of the mouth, which presumably contain the fusospirochetal organisms, were present below the glottis in 155 of 200 cases investigated.

The opportunity for aspiration is lessened in operations outside the buccal cavity, and there is a corresponding diminution in the incidence of pulmonary abscess. At Ray Brook we have had two putrid abscesses following clean herniotomies in which spirochetes were found in the foul sputum. In these cases the organisms must have reached the lung from the mouth by way of the trachea. Abscess of the lung without a preceding history of operative trauma is probably fairly common. In one month at Bellevue I saw eight such instances. There is little room for doubt that here the infection travelled along the respiratory channels.

It does not seem logical to consider that the infection is carried by the vascular route in bronchiectasis, for the disease so frequently begins as an insidious bronchitis. Yet bronchiectasis is the most common fusospirochetal lesion in the lung. Moreover, in Vincent's angina, secondary lesions have been discovered in the trachea and bronchi, which is substantial proof that in these instances the air passages transmitted the infection to the lung.

The vascular theory does not offer a satisfactory explanation for the protean clinical manifestations which characterize fusospirochetal infections of the lung. The experimental work of David Smith has conclusively proved that the symbiotic fusospirochetal group of organisms fulfils Koch's postulates for the causative factor of pulmonary abscess and its allied conditions. This group of organisms is found in the buccal cavity. Its invasion of the lung is undoubtedly by the direct route of the open trachea and bronchi.

DR. E. C. CUTLER: I agree with Dr. Bray that bronchiectasis is the more common disease. I wish to emphasize, however, that I was not speaking of bronchiectatic abscesses. These two disorders, the bronchiectatic and the parenchymatous abscess, are entirely different.

Our insufflation experiments were conducted by injections into the trachea. This is different from injections across the neck into the trachea as carried out at the Ray Brook Hospital by Dr. Smith and Dr. Bray. The great opportunity for vascular or lymphatic infection in this method has been emphasized. I should like to point out again that the successful experiments in many other pulmonary disorders are open to the same criticism, viz., that direct translaryngeal experiments have failed whereas transbronchial injections have succeeded.

I should like again to speak of the operation of tonsillectomy and the supposed high incidence of abscess following this. So far as we know 50 per cent of the cases of abscess of the lung follow tonsillectomy. But this operation constitutes about 50 per cent of all surgical procedures in a septic field.

I admire greatly the ingenious work of Dr. Bray and his associates. I do believe that aspiration of buccal contents is of normal occurrence though this may not go on continuously and may be more active in sleep.

I thought that I was generous in explaining this matter by crediting the proponents of the aspiration theory with the important factor of chronicity, but I find that they demand aspiration as the total and sole etiologic factor to refute which we have brought the experimental work and clinical observations already cited.

CHICAGO PEDIATRIC SOCIETY

Clinical Meeting, April 16, 1929

A. LEVINSON, M.D., *Chief of Staff, Presiding*

ACUTE OSTEOMYELITIS, WITH COMPLETE SEQUESTRATION OF THE LONG BONES. Presented by DR. HARRY JACKSON.

A girl, aged 7, entered the hospital with a history of pain, fever, leukocytosis and inability to use one arm for a period of four days. The arm was swollen from the elbow to the shoulder, and the patient was admitted with a diagnosis of cellulitis of the arm. The pain was most marked at points near the shoulder and the elbow. A roentgen examination made before the child entered the hospital gave negative results, as did the first one in the hospital, but a diagnosis of acute osteomyelitis was made in spite of the negative observations, because of the extreme tenderness to finger-tip pressure near the ends of the bone. Openings were made at both the upper and the lower ends of the humerus, and the periosteum was found to be slightly raised and pus exuded from the drill holes in the bone. At the end of about four weeks the entire humerus formed a sequestrum, with the beginning of an involucrum, and at the end of about ten weeks a complete involucrum had formed from the periosteum. The entire humerus was removed through an incision from the tip of the shoulder to the elbow, through the muscle planes and through a groove chiseled out of the involucrum. There was some osteomyelitis at the elbow joint and the upper portion of the ulna. The child made a complete recovery, with formation of a new humerus.

At that time complete wrist-drop was noted, and a third operation was done in which the radial nerve was exposed, found to be embedded in the involucrum and pinched off. The bone was chiseled away from the nerve and found to be severed; the ends were freshened and brought together with fine catgut sutures. In six months regeneration of the nerve had taken place, and after that time function of the arm increased until it was practically normal. The child still had a little difficulty in completely extending the arm, due to some changes in the elbow joint, but the shoulder joint was entirely free.

During the last three years, there have been four cases of complete destruction of the long bones of the extremities in this hospital: one of the ulna, one of the humerus, one of the tibia and one of the radius. The child in whom the tibia was affected had not been seen by a physician for a year, and the bone was protruding through the skin and could be lifted out easily when he was brought into the hospital.

The interesting question is whether a new bone marrow forms in these cases where the new bony growth takes its origin entirely from the periosteum. There have been a number of cases in this hospital in which several of the long bones have been involved at one time, so that from 60 to 70 per cent of the bone marrow

has been destroyed. This interferes markedly with the formation of blood, and may have some influence on the growth of the child and of the blood cells, particularly the white blood cells.

If it were possible to see the patients with osteomyelitis early so that they could be operated on before marked destruction of the medullary cavity has occurred, it would be ideal. The only pathognomonic sign is revealed by finger pressure over the ends of the metaphyses of the long bones. If the pressure is continued for three or four minutes, the child will cry out with acute pain. In no other disease does finger pressure cause acute pain localized to one finger point, which increases as the pressure is continued. If one is called to see a child with a rise in temperature and pain in an extremity, and finds excessive tenderness proximal to the joint which increases on continued pressure, in spite of the fact that the roentgen examination gives negative results and there are no other manifestations, one should not permit the condition to go on without at least making an opening into the bone.

RICKETS AND THE THYMUS. Presented by DR. I. H. TUMPEER.

In discussing Aldrich's recent paper on the significant occurrence of smooth muscle spasm in infants with large thymus glands, Tumpeer corroborated this observation from his own data, and mentioned that significant bone changes resembling rickets also were found in many of this group, with no lack of the usual antirachitic factors such as breast feeding, cod liver oil, sunlight and good hygienic surroundings. In this exposition, he demonstrated patients with craniotabes and funnel breast who had manifested so-called pylorospasm and choking spells, respectively, and who were relieved by roentgen irradiation of the thymic area. On presenting case histories of smooth muscle spasm of various types, he demonstrated roentgenograms of the thymus and long bones illustrating the association of bone changes resembling rickets with an enlarged thymus in infants without avitaminosis in whom the dietetic and hygienic factors had been satisfied.

He offered the following suggestive observations: Before he had become aware of the thymic factor, he had noted and recorded that infants with so-called pylorospasm consistently developed craniotabes at the age of 4 months. The coincidence of smooth muscle spasm and bone changes compels a comparison with the entity known as spasmophilia. The frequency with which many of these infants pass from one manifestation to another of the so-called spasmophilic diathesis and exudative diathesis suggests the possibility that some fundamental physiologic truth may be uncovered.

DISCUSSION

DR. C. A. ALDRICH: I am interested to know that Dr. Tumpeer has found the vagotonic symptoms in his series, as I have. I have not kept definite records in respect to the incidence of rickets and cannot say what percentage of these children have had rickets. It would be interesting if one could secure such a percentage of incidence in a large series.

DR. I. H. TUMPEER: The percentage of infants with enlarged thymus who manifest bone changes is not at hand. It is my impression that a surprisingly large number of these infants present the changes usually called rickets. The percentages are not as important as the fact that in infants with enlarged thymus who live under the most hygienic surroundings and whose dietary contains an abundance of the antirachitic vitamin, rickets develops.

THROMBOCYTOPENIA-PURPURA (TREATED BY REPEATED BLOOD TRANSFUSIONS AND SPLENECTOMY). Presented by DR. J. H. HESS.

A white girl, aged 8 years, was admitted to the hospital on Feb. 25, 1929, complaining of hemorrhagic spots on the extremities and chest, and attacks of severe epistaxis. Two weeks before admission, she had a "cold" and with it had several slight nosebleeds. A few days later, about February 17, she had a severe nasal

hemorrhage lasting for several hours. At the same time the parents first noticed a few hemorrhagic spots the size of pinpoints on the extremities. On February 23, she had a second severe nasal hemorrhage that started at midnight and continued until 8:00 a. m. on February 24. A third severe nasal hemorrhage began during the afternoon of February 24 and continued until the child was admitted to the hospital on February 25, about 3:00 p. m.

The past history was unimportant except for an attack of bleeding in 1926 that was similar but not nearly so severe as the present one. The family history was unimportant.

Abdominal examination gave negative results. No organs or masses were palpable, and the liver and spleen did not seem to be enlarged. There was a soft systolic murmur with no cardiac enlargement.

Following admission, 40 cc. of whole blood was injected into the muscles of the thigh. This was repeated on February 27. On March 1, a large hematoma appeared at the site of the first injection, and there were profuse bleeding from the wound and epistaxis. The child was again given 40 cc. of her father's blood into the buttocks and calcium lactate internally, 40 grains (2.6 Gm.) daily. The father's blood had been used in each of these three intramuscular injections without visible effect.

On March 4, the nasal hemorrhage was so severe that it was necessary to make a postnasal pack. The red cell count had dropped to 1,800,000, with a hemoglobin content of 55 per cent. Polychromatophilic and basophilic stipple cells were present. The bleeding time was nineteen minutes. The white blood cells numbered 15,200, with 86 per cent polymorphonuclear cells, 10 per cent lymphocytes, and 4 per cent mononuclears. On three previous examinations a few platelets were present, but on March 4 none could be demonstrated.

On March 5, 180 cc. of the father's blood was given intravenously. Following this injection, the petechial hemorrhages disappeared, but for only a short time. On September 8, because of recurrent hemorrhages and petechiae, 275 cc. of whole blood from a professional donor was given intravenously. On the 12th, she was given 200 cc. intravenously from the same donor. On the 14th, numerous fresh petechiae appeared on the face and trunk.

Repeated hemorrhages, notwithstanding repeated transfusions, led the physicians to recommend splenectomy. On March 27, following transfusion of 250 cc. from a professional donor, immediately preceding the operation, the spleen was removed. The left jugular vein was used for the transfusion.

The spleen was moderately enlarged, fairly soft in consistency and showed no abnormalities in appearance except for adhesions between the tip of the pancreas and the hilum of the spleen. During the operation, the tissues showed little more than the normal tendency to hemorrhage. The liver was apparently normal in size and appearance and showed no evidence of cirrhosis. The patient left the operating table in good condition. Except for a rise in temperature which could be accounted for by a superficial abscess of the wound, the patient made an uneventful recovery. There was no tendency on the part of the abdominal wound or the jugular incision to bleed.

The result to date has been especially gratifying, because of the statistics which give a high postoperative mortality for splenectomy performed during the acute stage or in acute cases of thrombocytopenic purpura.

A summary of the examinations of the blood is of great interest. The coagulation time, which at first was three and one-half minutes, gradually increased to sixteen minutes preceding the operation, remaining uninfluenced by the various transfusions, but dropped to eight minutes on the day following and within three days to two minutes; since which time it has not risen above two and one-half minutes. The bleeding time, which on first examination was eight and one-half minutes, increased to two hours and forty minutes before operation, and since the operation has averaged between three and six minutes.

Expressed in terms of thousands, the minimum number of polymorphonuclear cells was about 3,500 on the twelfth day after admission, 4,200 on the day preceding

the operation and 33,800 on the day following the operation. The minimum leukocyte count since the operation was 12,600.

The red blood cells at one time dropped to 1,830,000; at the present time, there are 3,500,000. The platelets before operation ranged between a complete absence to so few that their number could not be estimated with accuracy. On the day following the operation, there were 68,000; on the fourth day, these dropped to 14,000; on the fifth day, they rose to 40,000, on the eighth day to 247,000; on the thirteenth day, they dropped to 106,000 and since that time have fluctuated between 35,000 and 105,000.

Immediately following removal of the spleen, a splenic puncture was done, and the splenic pulp was shown to contain large numbers of thrombocytes. An interesting observation was the finding of the so-called giant thrombocytes. The average size of the blood platelets was between 2 and 3 microns. In the slide made from the material obtained on splenic puncture, the platelet shown has a diameter several times greater. That these cells were active was demonstrated by the presence of fibrin threads emerging from the platelets.

Summary.—In essential purpura hemorrhagica, depending on their reaction to splenectomy, two large groups are to be considered, and these are based on the presence or absence of normal activity of the bone marrow. In other words, is there an extramedullary destruction of blood platelets by the spleen with normal activity of the marrow or is there a failure of the blood element centers in the marrow resulting in aplasia and fatty degeneration? The favorable case belonged to the first group as evidenced by the neutrophilic response to hemorrhage and transfusion and the condition of the spleen.

AURICULAR FIBRILLATION. Presented by DR. PHILIP ROSENBLUM.

A boy, aged 8 years, had a history of frequent attacks of tonsillitis and rheumatism. At the age of 2½ years he developed a double mitral lesion, and the year before presentation he was in the hospital for five months with chorea. The fibrillation was first noted eight months before presentation; two months before presentation he had a recurrence, because of an infection of the upper respiratory tract, but it responded readily to rest in bed and digitalis.

A girl, aged 14 years, developed tonsillitis and rheumatism at the age of about 3 years. She was in the hospital with fibrillation three years before presentation; she has had fibrillation since then, but has been able to get about during the entire period.

Both of these children have fibrillation now but are fully compensated and able to get about. They both had rheumatism and a double mitral lesion. The girl did not show the presystolic murmur, as would be expected, but the absence of the murmur does not exclude mitral stenosis. When she was seen, about two and a half years ago, she had a pulse deficit of about 200 beats, with a cardiac beat of about 310 and a pulse of 110 at the wrist. This usually indicates serious myocarditis, as it is usually associated with sclerotic processes in the myocardium.

The prognosis, while serious, shows that these patients with auricular fibrillation can get about for a long period.

PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. Presented by DR. J. K. CALVIN.

A boy, aged 11, first noticed the symptoms of the disease when he was 6 years old. There is no hereditary or familial history of the condition, and he apparently was perfectly well until he was 6. The early symptoms were the usual ones of difficulty in walking, and within a year and a half he was entirely unable to walk. About that time the usual symptoms manifested themselves in the arms, and he now presents a typical picture of the disease.

This boy's difficulty began at the age of 4 years, and at the time of presentation he was about 10. He did not walk until he was 2½ years old; then he walked with some difficulty for about a year and a half, when symptoms much the same as the first boy showed appeared.

These two cases are so similar that they are interesting. After six years' duration, the condition in both is at about the same stage. Neither of the boys can sit up without a back-rest; neither can walk, and both have developed the contractures or talipes of the lower extremities. The first boy can still move his fingers and toes, can move his arms with great effort by a peculiar maneuver, but seems to have no difficulty in moving his neck. He can chew well and can move his eyes, but his smile is transverse. There is also evidence of atrophy of the facial muscles, which causes a masklike expression.

In the second patient, because of the wrist-drop over a long period, an arthrodesis was done so that he could hold his hands out, and in that way he was enabled to grasp objects in some positions.

There are no sensory changes, no loss of sphincter control and no mental deterioration. As far as can be determined, there is no involvement of the central nervous system. The knee and Achilles jerks are absent. The reflexes in the arms are sluggish. Both boys are quite obese; the first weighs 108 pounds (49 Kg.) and has almost doubled his weight in the last two and a half years, the fat replacing muscle tissue throughout the body.

Because of the general fatty deposits all over the body, an attempt was made to study the basal metabolism. Three or four tests were made, which varied from 2+ to 4+. The sugar tolerance, tested at various intervals during three years, has been normal each time. There is no disturbance in the carbohydrate metabolism or the basal metabolism. Biopsy shows that the muscular tissue is almost absent and replaced by fatty deposit and connective tissue.

Cultures were made of the excised tissue, but no organisms were found. Repeated cultures from the nose and throat have shown *Streptococcus viridans*, and on repeated blood culture these organisms were found once. Streptococcic vaccine has been administered, but the condition has continued to progress. Whole suprarenal gland and strychnin in large doses have been administered, without any improvement in muscle tone. Also, a high carbohydrate diet, combined with insulin, has been tried, but has been of no avail.

In spite of the author's efforts, nothing has been revealed on the etiology or therapy of these cases.

CLINICAL ASPECTS OF APPENDICITIS IN CHILDREN. DR. HAROLD FREEDMAN.

From the study of forty-two cases of appendicitis in children admitted to the Sarah Morris Memorial Hospital during two months in the summer of 1928, the following conclusions were drawn: 1. Perforation is more frequent in earlier years. 2. The white blood cell count, the temperature and the pulse rate are, on the average, higher in appendicitis in which rupture occurs than in acute appendicitis. 3. The extreme ranges which the white blood cell count, the temperature and the pulse rate may take make them of little contributory value as far as differential diagnosis is concerned. 4. Nausea and vomiting are usually found in acute appendicitis, and are practically always found in appendicitis in which rupture occurs. 5. Diarrhea is rare and constipation quite common. 6. A leukopenia may be indicative of a severe toxicity. 7. Postoperative discomfort is reduced in toxic cases by the administration of saline hypodermoclysis. 8. Appendicitis may possibly occur as a consequence of acute infection of the upper respiratory tract. 9. Localized tenderness and spasm are more important than any other clinical signs in the diagnosis of appendicitis.

UROLOGIC CONDITIONS IN CHILDREN. Presented by DR. D. N. EISENDRATH.

By means of lantern slides and pathologic specimens, several interesting urologic conditions encountered in children were demonstrated.

APPARATUS FOR ADMINISTERING DEXTROSE SOLUTION. Presented by DR. W. THALHIMER.

Dr. Thalhimer presented and described the apparatus he had devised for administering dextrose solution at almost any desired speed, a description of which has been published in THE JOURNAL of the American Medical Association.

CLEVELAND ACADEMY OF MEDICINE, SECTION ON PEDIATRICS

C. L. Ruggles, M.D., *Reporter*

Meeting, April 24, 1929

C. W. Wychoff, M.D., *Chairman*

Problems of the Pediatrician as the Psychologist Sees Them. Dr. Garry C. Meyers.

In Dr. Meyer's opinion, a large part of the pediatrician's success depends on how well the child is guided in the home and on the degree to which he can cultivate parental guidance. His paper urged the early teaching of the meaning of "no," with the infliction of pain in an impersonal manner to develop specific inhibitions limited to a few important situations. Such punishment must be immediate, in direct proportion to the transgression, and must be put in effect on the first and on each subsequent occurrence consistently. Too little emphasis has been placed on training the child so as to allow others to express themselves and their individuality. The pediatrician must not discourage the mother by blaming her errors for the child's faulty habits, but must tactfully correct her mistakes in a constructive way. This should be done at the time of prophylactic consultation with the mother in a receptive mood rather than on the occasion of an illness which has already disturbed her mental balance.

Functional Disorders in Childhood. Dr. Oscar B. Markey.

Dr. Markey stated that all unexplained symptoms are usually relegated to the functional group without further attention. All symptoms are regarded as functional in the absence of demonstrable organic causes. None are controlled consciously by the will, except temporarily, because function lies below the level of consciousness. Efforts to control function make the individual function-conscious, and functional disorders inevitably occur. The following important disorders were discussed. Those of appetite and digestion are begun in early infancy, when frequent dietary changes are made in the presence of unimportant symptoms and overanxious mothers until the formula "food plus mamma" equals "fight." Children should have the major responsibility in a limited choice of foods, and outside emotional influences should be minimized or absent. In enuresis organic causes should be looked for from time to time even after they have been ruled out. Fallacious "causes," such as weak kidneys and the expectation that puberty will bring a cure, act as a license for continuing the habit. Chronic enuretic children almost always have other problems in the emotional field. In the presence of emotional disorder, two main types of speech difficulty may occur, disturbance of rhythm, namely, stammering and stuttering. These children are usually mouth conscious because of repeated reminders. Infantile enunciation is a powerful means of retaining the importance of infancy. Harmonious environment and an absence of reminders are the essentials of therapy.

Fatigue, restlessness, irritability, instability and emotional explosion cause each other in a vicious cycle in the order named. A rich environment is required to satisfy such children, but patterns of rest and routine are important. Tics, habit spasms and the like occur originally as a response to an irritant, but continue as a habbit after the irritant has disappeared; reminders are harmful. Emotional calm is needed, and in many cases muscle reeducation centering around diaphragmatic breathing is helpful. Serious mental problems are uncommon in childhood and represent the need of psychiatric approach almost entirely. Examples of these were described. In conclusion it was shown that functional disorders prove the importance of nonorganic causes which can be found through study of the environment, the intelligence and the emotional make-up of the child.

Book Reviews

THE CHILD OF CIRCUMSTANCE. By ALBERT WILSON. Price, $6. Pp. 413, with illustrations. New York: William Wood & Company, 1929.

The author of this book is an eminent English physician who has been interested in criminology for the greater part of his medical career. His early training under Sir Frederick Mott and others led to prolonged investigations in criminology from the physiologic and the pathologic point of view. This book presents a general discussion of crime from the scientific point of view.

The book contains more than 400 pages. Crime is extensively discussed from the standpoint of heredity. "The real reason (for crime) is the loss of inhibition through nondevelopment of the brain." Physical inferiority, including maldevelopment, congenital syphilis, abnormal endocrines and alcoholism in the parents, is stressed. Psychopathic personality, insanity, feeblemindedness, sex perversions and abnormal family traits are included in the most frequent factors contributing to crime. Much space is utilized in severely criticizing the contributions of the modern psychologists and psychiatrists. Psychoanalysis and everything contributed by the Germans is most severely criticized. Mental tests and American psychology and psychiatry are criticized or ignored. The author's treatment of criminals and prevention of crime may be summarized in two sentences: "We must urge the importance of careful treatment of all children who have had any brain trouble and the treatment must be rest, quiet (?) ultraviolet rays and nonstimulating foods. As a strong advocate of emotional religion for the weak minded, uneducated and degraded I am prepared to justify my position."

Capital punishment and penal institutions are extremely well discussed. The author gives most interesting and extensive descriptions of penal institutions throughout Europe with constructive as well as destructive criticisms.

The subject matter is arranged in an incoherent manner, but is made interesting by a large number of case histories. The book is concerned largely with adults. There is little discussion of child psychology.

This book would be of special interest for the general information of a previously uninformed layman. It stresses the older points of view but does not give adequate consideration to present day psychology and psychiatry as applied to criminology.

OSTEOMYELITIS AND COMPOUND FRACTURES. By H. WINNETT ORR. Price, $5. Pp. 202, with illustrations. St. Louis: C. V. Mosby Company, 1929.

In this volume, the author lays the foundation for and describes his method of treatment of infected wounds, especially of bones and joints. The subject matter is well presented and illustrated.

He reviews the teachings of the old masters, such as Hilton, Thomas and Lister. Hilton recognized the importance of rest in treating infected wounds, while Thomas devised the methods and appliances to make this treatment possible. Lister recognized the importance of antiseptics in preventing infection rather than in treating infected wounds.

The author's experience in the late world war taught him that too much emphasis was placed on the treatment of the wound and too little on the position of the limb and the possibility of deformity and disability.

A review and discussion of the present methods of treatment of compound fractures and osteomyelitis show how unsatisfactory they are. His own method of treatment is based on wide open drainage, immobilization in a functionally correct position and infrequent dressings. His work is supported by numerous cases from his own clinic, as well as from those of others. In studying his case

reports, one is impressed with the lack of complications, the good functional results and the fact that other surgeons have had the same success with the method as the author has had.

RICKETS, INCLUDING OSTEOMALACIA AND TETANY. ALFRED F. HESS, M.D. Price, $5.50. Pp. 485, with 52 engravings. Philadelphia: Lea & Febiger, 1929.

This book is the last word on rickets. The etiology, pathology, metabolism and pathogenesis are fully discussed. Throughout the book, results obtained experimentally in the laboratory have been weighed and appraised in the light of clinical experience, and whenever there have been discrepancies or disagreements, the clinic has been adjudged the final arbiter. This work is made more complete by added chapters on osteomalacia, late rickets and tetany. The chapters on symptoms, diagnosis and prognosis are full and conclusive. The book is exceptionally well written and easy to read. One reason for this is the lack of attempt at bibliographic display. The bibliography is complete and extensive, but is arranged according to chapters at the end of the book. This book should be of exceptional value to the practitioner and clinician, as well as to the nutrition worker.

KLINISCHE GASSTOFFWECHSELTECHNIK. By DR. H. W. KNIPPING and DR. H. L. KOWITZ. Paper. Price, 18 marks. Pp. 193, with 74 illustrations. Berlin: Julius Springer, 1928.

This excellent little book has been compiled by the authors in order to make available a handbook that will be useful in metabolism determinations. It discusses the various types of apparatus, their use and the methods of using them, and contains useful tables of the reductions of gas volume at different temperatures and at a pressure of from 621 to 760 mm. of mercury, as well as the Harris Benedict formula for estimating the normal metabolism, and other similar tables. It does not pretend to discuss the theoretic aspects of metabolism.

Directory of Pediatric Societies

INTERNATIONAL

INTERNATIONAL CONGRESS ON PEDIATRICS

Prof. I. Jundell, Artillerigatan 23, Stockholm, Sweden.
Place: Stockholm. Time: Aug. 17-20, 1930.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON DISEASES OF CHILDREN

Chairman: Dr. William Weston, 1231 Bull St., Columbia, S. C.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Detroit. Time: 1930.

AMERICAN PEDIATRIC SOCIETY

President: Dr. Joseph Brennemann, 30 N. Michigan Blvd., Chicago.
Secretary-Treasurer: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Montreal. Time: May or June, 1930.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. Lawrence T. Royster, State Board of Health, University, Va.
Secretary: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 7th Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 7th Ave., New York.
Place: Minneapolis. Time: Sept. 30-Oct. 4, 1929.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. Thomas Crossan Clark, 51 Herkimer St., Hamilton, Ont.
Secretary-Treasurer: Dr. Frank H. Boone, 164 James St. S., Hamilton, Ont.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. J. Gurney Taylor, 120 E. Wisconsin St., Milwaukee.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.
Place: Milwaukee. Time: Sept. 27-28, 1929.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

Chairman: Dr. J. H. Eugene Rosamond, 1074 Madison Ave., Memphis, Tenn.
Secretary: Dr. A. J. Waring, De Renne Apts., Savannah, Ga.
Place: Miami, Fla. Time: Nov. 20-22, 1929.

LOCAL

ALABAMA PEDIATRIC SOCIETY

President: Dr. J. MacBell, Mobile.
Secretary-Treasurer: Dr. Hughes Kennedy, Jr., Highland Plaza Apts., Birmingham.

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. Edward B. Shaw, 384 Post St., San Francisco.
Secretary-Treasurer: Dr. Lloyd Hardgrave, 384 Post St., San Francisco.
Place: Various teaching schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Ezra S. Fish, Pacific Mutual Bldg., Los Angeles.
Secretary: Dr. Fred L. Glascock, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. Elsie Seelye Pratt, Republic Bldg., Denver.
Secretary-Treasurer: Dr. Wilford W. Barber, Metropolitan Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month from September to May, inclusive, 2:30 p. m.

GEORGIA PEDIATRIC SOCIETY

President: Dr. W. N. Adkins, Medical Arts Bldg., Atlanta.
Secretary-Treasurer: Dr. E. N. Gleaton, 212 E. Gaston St., Savannah.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

Chairman: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Secretary: Dr. William Kiser, Medical Arts Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St. Time: Second Thursday of each month from October to April, 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. Edwin T. Wyman, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Randolph K. Byers, 66 Commonwealth Ave., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Arthur H. Parmalee, 310 S. Michigan Blvd., Chicago.
Secretary: Dr. Bert I. Beverly, 130 S. Oak Park Ave., Oak Park, Ill.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. J. A. Crawford, Lake Charles.
Secretary-Treasurer: Dr. C. T. Williams, 7401 Burthe St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. M. Boyd Kay, 10 Peterboro St., Detroit.
Secretary: Dr. Charles A. Wilson, 71 E. Ferry St., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. C. R. Moriarity, La Salle Bldg., Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester, Minn. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. Park J. White, Beaumont Bldg., St. Louis.
Secretary-Treasurer: Dr. Ralph L. Cook, 508 N. Grand Blvd., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Pkwy., Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. L. H. Barenberg, 1749 Grand Concourse, New York.
Secretary: Dr. Joseph Golomb, 496 E. 175th St., New York.
Place: Concourse Plaza, 161st St. and Grand Concourse. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Fourth Thursday of October, January and April.

NEW YORK ACADEMY OF MEDICINE, SECTION OF PEDIATRICS

Chairman: Dr. F. Elmer Johnson, 300 West End Ave., New York.
Secretary: Dr. Hugh Chaplin, 39 E. 75th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

ROCHESTER PEDIATRIC SOCIETY

President: Dr. John Aikman, 184 Alexander St., Rochester, N. Y.
Secretary: Dr. Howard F. Rowley, 278 Alexander St., Rochester, N. Y.
Place: Arranged by program committee. Time: First Friday of each month from October to May.

ACADEMY OF MEDICINE OF CLEVELAND, PEDIATRIC SECTION

Chairman: Dr. C. W. Wyckoff, 8314 Euclid Ave., Cleveland.
Secretary: Dr. C. L. Ruggles, 10616 Euclid Ave., Cleveland.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

OKLAHOMA STATE PEDIATRIC SOCIETY

President: Dr. William M. Taylor, Osler Bldg., Oklahoma City.
Secretary: Dr. Carol Pounders, 110 W. 10th St., Oklahoma City.
Place: Shawnee. Time: May, 1930.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Ralph M. Tyson, 334 S. 21st St., Philadelphia.
Secretary: Dr. John D. Donnelly, 115 Bryn Mawr Ave., Bala-Cynwyd, Pa.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to June, inclusive.

PITTSBURGH PEDIATRIC SOCIETY

President: Dr. Zaccheus R. Scott, Westinghouse Bldg., Pittsburgh.
Secretary: Dr. Theodore C. Elterich, Highland Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months.

THE SOUTH CAROLINA PEDIATRIC SOCIETY

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Place: Memphis General Hospital. Time: Second Tuesday of each month.

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Place: Westmoreland Club, 601 E. Grace St. Time: First Thursday of each month (other than during the summer).

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Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

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President: Dr. G. A. Davis, 12 Belsize Drive, Toronto.
Secretary: Dr. Gladys Boyd, 56 DeLisle St., Toronto.
Time: November 17, December 15, February 16 and March 15.

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